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The Journal of Laboratory and Clinical Medicine

VOL. IV. ST. LOUIS, DECEMBER, 1918 No. 3

ORIGINAL ARTICLES

REPORT OF EPIDEMIC OF "SPANISH INFLUENZA" WHICH OCCURRED AT CAMP A. A. HUMPHREYS, VA., DURING SEPTEMBER AND OCTOBER, 1918*

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INTRODUCTORY

THE great pandemic of "influenza" invaded Camp A. A. Humphreys, Virginia, during the second and third weeks of September and continued until the third week in October, covering a period altogether of about five weeks. The morbidity and mortality experience for this period may be summed up briefly in the following figures:

Average strength of camp,	26,600
Number cases influenza,	4,237
Number cases pneumonia,	1,171
Number deaths from pneumonia and influenza,	413

On the basis of the above figures we may derive the following pertinent facts:

16% of camp had influenza.
28% of influenza cases had pneumonia.
10% of influenza cases died.
35% of pneumonia cases died.

This epidemic was therefore responsible for the death of 1.6 per cent of the population of this camp.

*Published by permission of the Surgeon-General's Office, Washington, D. C.

During the summer months there had been an occasional case diagnosed by regimental surgeons as "influenza." Probably some of these were severe "colds" and possibly some authentic cases of "influenza." These cases occurred as follows: Between July 1 and September 12 only two white organizations had any cases of "influenza." The 5th Regiment shows a record of 17 cases prior to September 12. There were 15 cases in this regiment during the month of August. The regimental surgeon, however, is of the opinion that most of these cases were colds, as none of them had a fever and the record shows they were only off duty for one day.

The 3rd Regiment reported one case of "influenza" on August 18. There were scattered cases among the colored organizations between September 1 and 11. The interval between these cases and what may be considered the new cases of the epidemic seem to preclude there being any connection between them, unless this disease, like others, is kept alive by carriers. Table I gives the data regarding "influenza" cases in the several organizations between September 1 and 12. So small a number of cases as these occurring at that time of the year in a command of the strength of Camp Humphreys should not have excited comment. However, between September 13 and 18, 134 cases were reported.

TABLE I

INCIDENCE OF NEW CASES OF "INFLUENZA" IN CAMP PRIOR TO EPIDEMIC
SEPTEMBER 1 TO 12, 1918

SEPTEMBER	1	2	3	4	5	6	7	8	9	10	11	12
ORGANIZATION												
3rd E. T. R.				1							1	1
5th E. T. R.												1
Casual Det.	2											
540th Ser. Bn.			1									
541st Ser. Bn.			1									
542nd Ser. Bn.	2											
543rd Ser. Bn.								1				
546th Ser. Bn.											1	2
547th Ser. Bn.										1		

It may be assumed that the epidemic began on September 13 and ended October 18. The early cases were practically confined to the 3rd Regiment, but as soon as these cases were known, all medical officers were notified of the impending epidemic and directed to take special precautions in diagnosing the cases and to take special steps in order to prevent the spread of the disease.

MEASURES USED TO CONTROL THE EPIDEMIC

The first measures taken to prevent the spread of the disease consisted of a circular addressed to all regimental and battalion surgeons, calling attention to the presence of the disease and calling for special reports each morning as to the number of cases. This was on September 18. On this day also, a popular article was displayed in the camp newspaper, telling what influenza is, its mode of transmission, and the means of prevention. (See Appendix A.)

On September 18 also, the Commanding General issued a memorandum calling attention to the seriousness of respiratory disease in the American Army. He ordered that beds be screened from each other by shelter halfs of tents. This memo also included a time schedule for lectures on respiratory disease, to be attended by each organization in camp. (See Appendix B.)

The lectures mentioned in this memo were given by the Camp Surgeon, and all organizations, except the colored battalions, the Officers Training School and the 3rd Regiment were visited. In these organizations the regimental surgeons were requested to make the necessary announcements.

On September 27, the Commanding General issued a memo advising the organization commanders to send men with colds to regimental surgeons for examination. (See Appendix C.)

On September 30, after consultation with the Surgeon-General's Office, the Camp Surgeon addressed a memo to regimental and battalion surgeons and surgeons of the Base Hospital, requiring that 100 square feet of floor space be provided for each patient, and that all men with colds should report twice a day for proper nose treatment. (See Appendix D.)

On the above date, the Commanding General issued a memo directing organizations to secure sheeting from the Quartermaster to be used as screens between beds. (See Appendix E.)

On October 3, the Commanding Officer issued a general order dealing specifically with crowding and living conditions in quarters, the fly question and the washing of mess kits. (See Appendix F.)

On October 3, an inspection of the camp was made by Colonel Chamberlain of the Surgeon General's Office. The Camp Surgeon has since that time received an unofficial report from the Surgeon-General's Office stating that the report made to the Surgeon General as a result of this inspection was highly satisfactory as to the methods adopted at Camp Humphreys for the handling of the epidemic. The following day, October 4, as the result of Col. Chamberlain's visit, the Camp Surgeon issued a circular addressed to medical officers, giving detailed information on the handling and care of the sick and convalescents, and on the care of quarters. (See Appendix G.)

On October 8, the Commanding General issued a memo limiting the crowding in tents and barracks and specifying certain measures to be taken to secure adequate ventilation, cleanliness, and freedom from flies in barracks. Further attention was drawn to laxity in cleansing dishes. Officers were warned to eliminate coughers at mess and in the Y. M. C. A. gatherings. Crowding in the Y. M. C. A. hall was also dealt with. Organization commanders were told to keep men out of doors as much as possible, to avoid giving them fatiguing exercise and to have them bathe at least twice a week. Further attention was called to the detection and examination and isolation of those with incipient colds. Mention was made of the antispitting rule. (See Appendix H.)

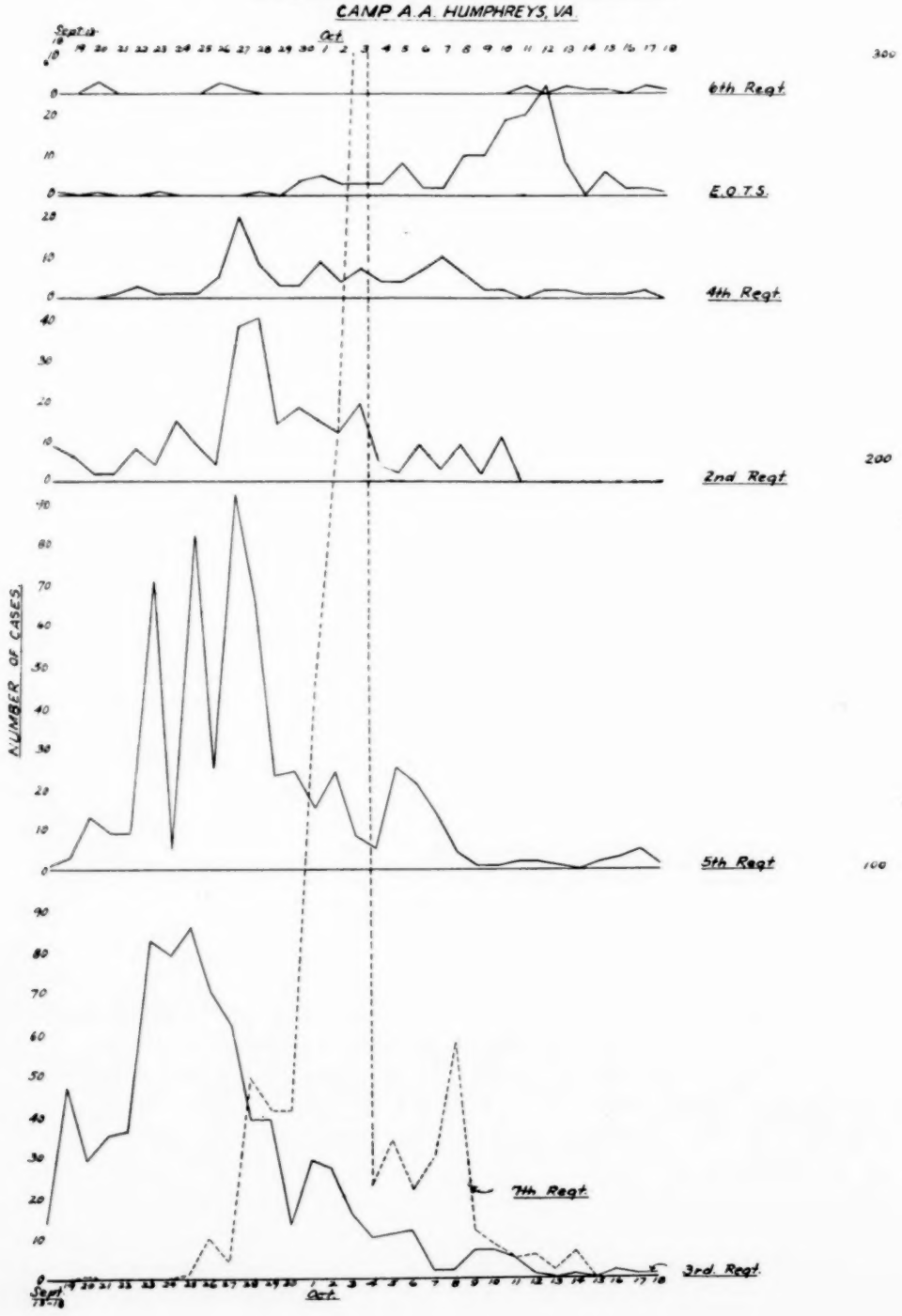
At no time during the epidemic was the camp under quarantine, and at no time were the men restricted in regard to their amusements. Although the Y. M. C. A. voluntarily omitted their usual entertainment features, the men

CHART 1.

INFLUENZA

Daily Record of New Cases in Various Regiments
During Course of Epidemic, Sept 13th-Oct 18th, 1918

CAMP A.A. HUMPHREYS, VA



were allowed to visit these buildings and the performances in the open-air theatre were continued throughout the epidemic.

During the first few days of the epidemic the Camp Surgeon visited the open-air theatre and various Y. M. C. A., Knights of Columbus, and similar buildings, and cautioned the men regarding spitting, explaining to them the importance of properly covering their faces while coughing or sneezing, and informing them as to the seriousness of the epidemic. It is believed these talks had a marked effect on the enlisted men.

At the beginning of the epidemic, verbal orders were given for the transfer of all influenza cases to the Base Hospital. As the epidemic progressed, and the cases became too numerous to be handled at the Base Hospital, it was necessary to open temporary hospitals in other parts of the camp. This was first done in connection with the 3rd Regimental Infirmary.

On October 4, Section J of the 3rd Regimental area was turned over to the Medical Department, in which a 500 bed hospital was established. This hospital annex was filled at once. It was evacuated October 27. Major Roscoe C. Hubbard, M.C., was in charge of the hospital annex, under the Commanding Officer of the Base Hospital.

PROGRESS OF EPIDEMIC

The epidemic lasted about five weeks and is summarized in Table II, which shows the number of cases developing each week during the epidemic and the percentage of the total. It will be seen from this table that the epidemic reached its maximum about the week ending October 4, when 52 per cent of the cases occurred. In all there were 4,237 cases up to, and including, October 18.

TABLE II

WEEKLY INCIDENCE OF NEW "INFLUENZA" CASES DURING THE FIVE WEEKS OF THE EPIDEMIC PERIOD OF SEPT. 13 TO OCT. 18, 1918

WEEK OF	NUMBER OF NEW CASES	PER CENT OF TOTAL CASES
Sept. 13-18	134	3.2%
Sept. 21-27	964	22.6
Sept. 28-Oct. 4	2208	52.2
Oct. 5-11	780	18.4
Oct. 12-18	151	3.6
Total	4237	100.

Table III shows the incidence of cases by days from September 13 to October 18. It also separates the cases according to color.

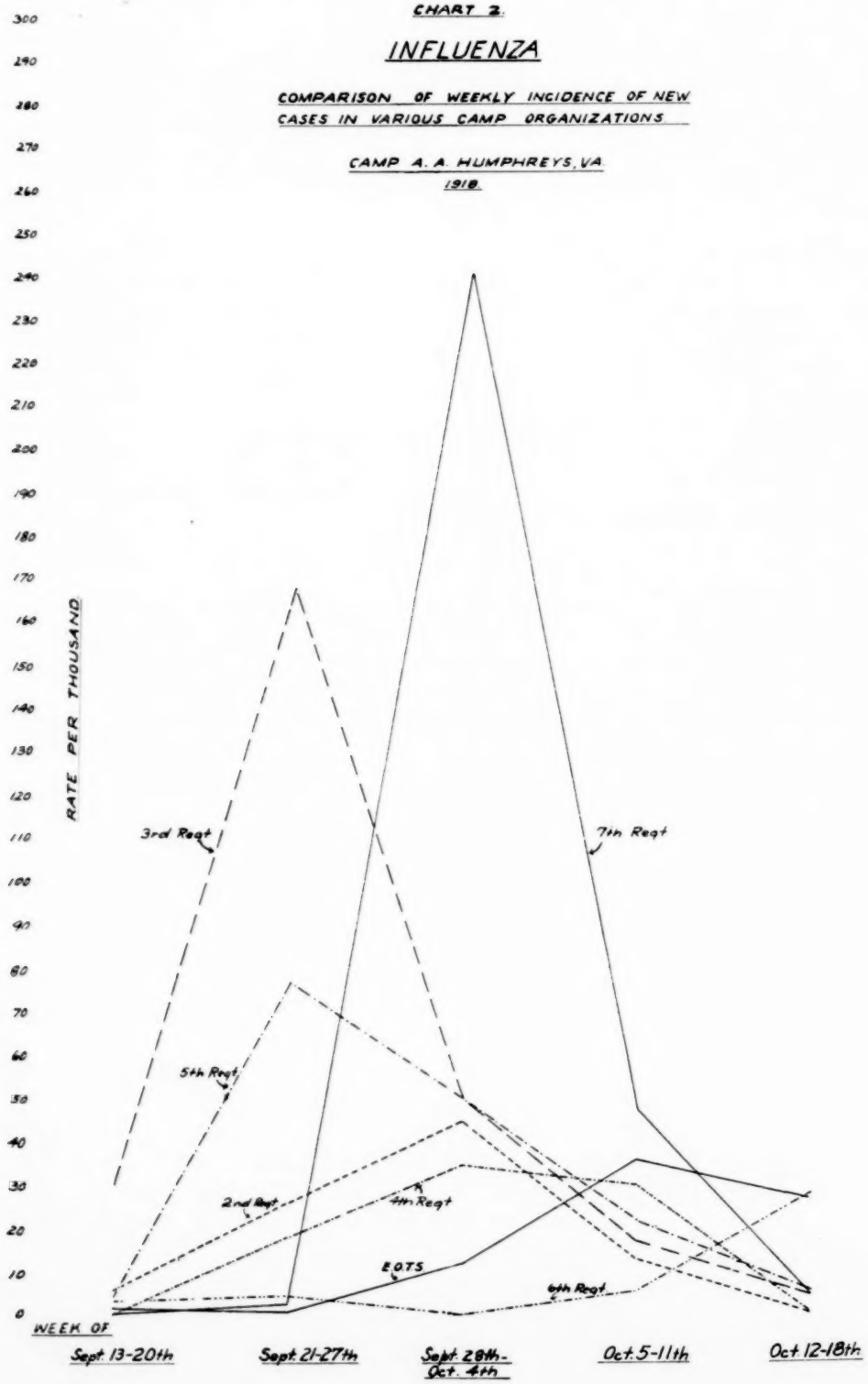
The data in Table III are shown in Chart 1. This is interesting in that it shows the waves of the epidemic in the different regiments. It also graphically shows the intensity of the epidemic in each organization. The lines appearing on this chart are the new cases each day in the various organizations. There are some fluctuations in the line, especially in the 5th Regiment, which are not readily understood, but are probably caused by clerical errors in reporting cases on the various days. From this chart it will be seen that the 3rd and 5th Regiments were infected almost simultaneously, and that the 3rd Regiment reached

CHART 2.

INFLUENZA

COMPARISON OF WEEKLY INCIDENCE OF NEW CASES IN VARIOUS CAMP ORGANIZATIONS

CAMP A. A. HUMPHREYS, VA.
1918.



its maximum on the 25th day of September, while the 5th Regiment did not reach its maximum until two days later. These maxima are almost practically coincident with the maxima in the 2nd and 4th Regiments. The 7th Regiment was affected somewhat later than the others, but suffered more severely. The maximum in that regiment was reached by October 3, and there was a secondary maximum about October 8. This may possibly be explained by the fact that

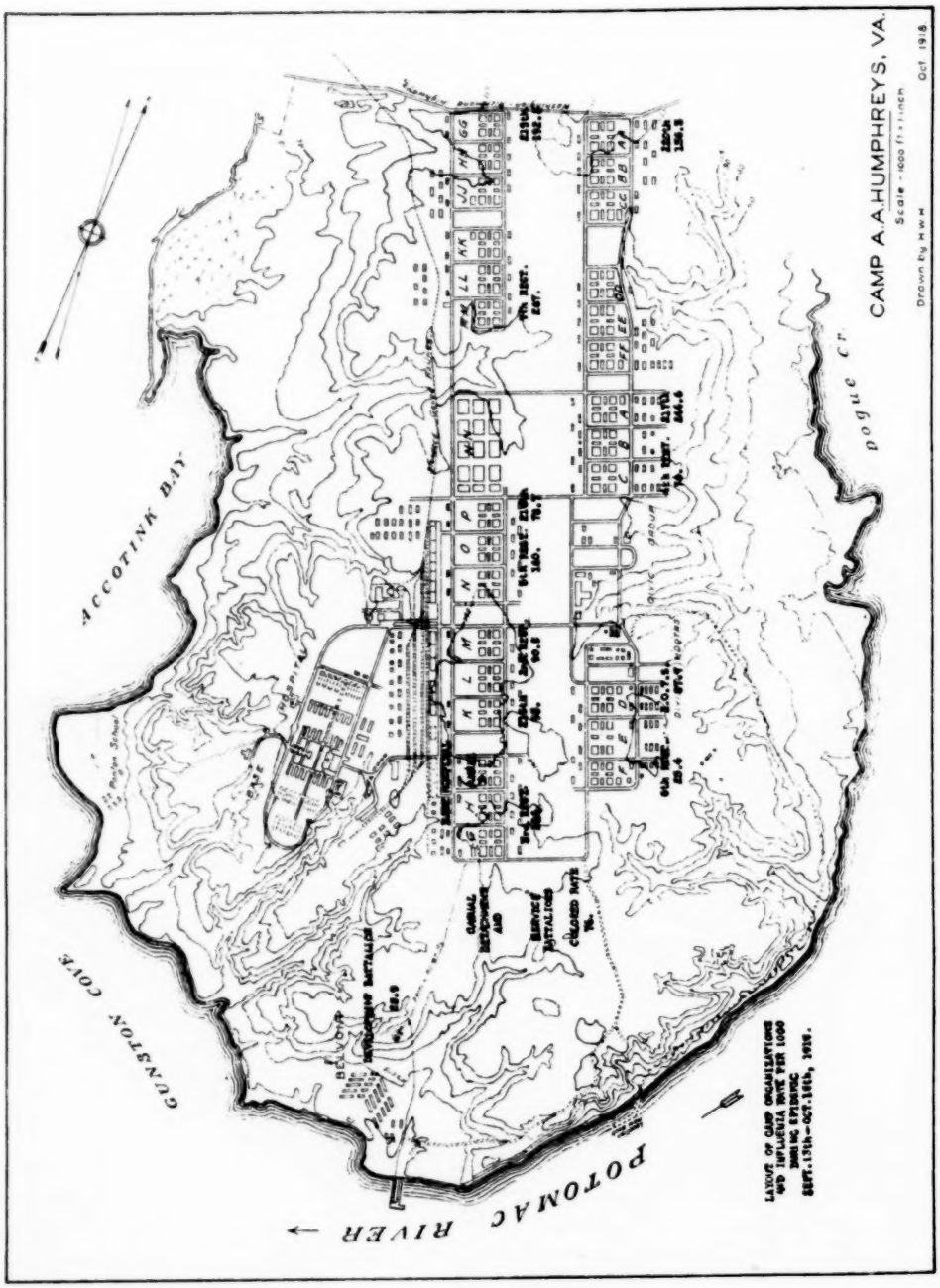
TABLE III

RECORD OF NEW CASES OF INFLUENZA, BY DAYS. WHITE AND COLORED SOLDIERS
PERIOD—SEPT. 13 TO OCT. 18, 1918

DATE	WHITE	COLORED	TOTAL
Sept. 13-18	25	4	29
19	56	0	56
20	49	0	49
TOTAL FOR WEEK	130	4	134
Sept. 21	47	1	48
22	56	0	56
23	160	3	163
24	100	6	106
25	179	8	187
26	117	19	136
27	239	29	268
TOTAL FOR WEEK	898	66	964
Sept. 28	206	35	241
29	125	26	151
30	148	29	177
Oct. 1	354	28	382
2	308	45	353
3	725	46	771
4	112	21	133
TOTAL FOR WEEK	1978	230	2208
Oct. 5	144	46	190
6	104	20	124
7	107	14	121
8	115	22	137
9	57	8	65
10	60	23	83
11	45	15	60
TOTAL FOR WEEK	732	148	780
Oct. 12	47	7	54
13	20	6	26
14	14	0	14
15	12	2	14
16	13	2	15
17	15	0	15
18	12	1	13
TOTAL FOR WEEK	133	18	151

between October 4 and 8 there were several regimental surgeons taken sick and the record may have become somewhat confused. This chart also shows the low incidence of the disease in the 4th Regiment, the Engineer Officers' Training School, and the 6th Regiment. This matter will be discussed more fully under another heading. Here it may be said that these regiments were provided with cubicles some weeks before the epidemic appeared and there was less crowding than in the other regiments, which is shown on another chart.

From the 13th to the 18th of September a total of 29 cases was reported,


CAMP A.A.HUMPHREYS, VA.
Scale - 1000 ft. = 1 inch
Oct. 1918
ACCOTINK BAY
pogue cr.
GUNSTON COVE
POTOMAC RIVER
←

half of these occurring in the 3rd Regiment. Most of these cases were reported on September 17 and 18. On September 19 only three organizations in the camp reported new cases, the total being 56,—46 of them being in the 3rd Regiment. On September 20 there was a total of 49 cases in seven organizations, 59 per cent being in the 3rd Regiment and 27 per cent in the 5th Regiment. In the second week of the epidemic the 3rd and 5th Regiments furnished about 80 per cent of the cases. During that week the epidemic spread to other organizations and increased very much. The third week of the epidemic marks the climax in most of the organizations, but the epidemic had already begun to decline in the 3rd and 5th Regiments.

Table III shows the incidence of cases by days from September 13 to October 18. It also separates the cases according to color.

CHART 3.

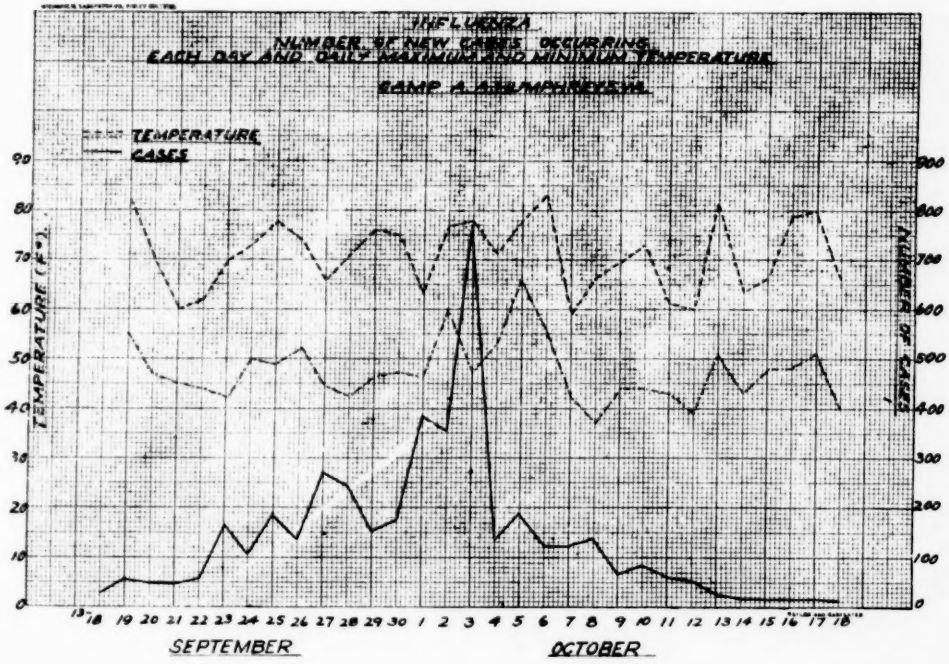


Chart 2 shows the weekly incidence of new cases in the white organizations, and is based upon rates per thousand as for the average strength of the command for these weeks. It shows that during the third week there was a general drop in all organizations except the 6th Regiment and the Engineer Officers' Training School. These two organizations suffered less severely from the epidemic than did the others and were somewhat later in infection. At the end of the 5th week the epidemic was still on the increase in these regiments, and the incidence in the Engineer Officers' Training School was relatively high. However, there was a decline during the following week and the epidemic practically disappeared in a few days after October 18. The largest number of cases in any day during the epidemic was 771 on October 3. Of these, 579 were reported

from the 7th Regiment. This organization had next to the highest incidence of any in the camp. It was natural to expect this as the men were not as well housed as were other organizations, and in addition they were all men who had been inducted into the service during September, among them being about 2,000 limited service men who did not possess the best stamina. The suddenness of the epidemic in the 7th Regiment is shown on Chart 1, the scale in that case being exactly the same as for the 3rd Regiment.

RELATION OF DUST AND WEATHER TO SPREAD OF INFECTION

During the epidemic there were many dusty days. This caused some comment among the officers and enlisted men of the camp and the inspector from Washington called attention to it, with a recommendation that some dust-laying preparation be sprinkled on the roads. The geographical distribution of the cases does not seem to indicate that dust was an active factor in the production of the disease. The service battalions, which are the closest to the 3rd Regiment and directly in line to receive their dust, did not suffer as greatly as did the 7th Regiment which is to the windward of the 3rd Regiment and at a considerable distance. (See map of camp.)

A number of persons have advanced the theory that the epidemic was due to weather conditions, laying emphasis on the mean temperature. Chart 3 shows the number of new cases each day, in solid lines, and in broken lines is shown the maximum and minimum temperatures as reported by the Weather Bureau in Washington. This is the Weather Bureau situated nearest Camp Humphreys. It will be seen from this chart that there is apparently no connection between the incidence of new cases and the weather conditions. The days on which there was the lowest temperature and the greatest range of temperature there were only a small number of new cases, nor was there an increase on the following days. The weather as a cause of disease has been overworked.

DISTRIBUTION OF CASES

The epidemic may be regarded as having started in the 3rd Regiment. The Engineer Officers' Training School and the 6th Regiment, which are directly across the parade ground from the 3rd Regiment, suffered very lightly from the epidemic. There is apparently very little intercourse between the members of these organizations and the 3rd Regiment. However, they would have been affected by the same atmospheric conditions as the 3rd Regiment, the prevailing winds being southerly. The location of these organizations is shown on the map of the camp.

Development Battalion No. 1, located at Belvoir, about one mile from the 3rd Regiment, shows a rate of 28.9 per thousand, which is one of the lowest in the camp. The low rate in this organization is without doubt directly due to the fact that the men there are practically quarantined, and there is very little mingling between them and the rest of the camp. An analysis of the 13 cases occurring in this battalion shows that 4 of them were men who had been in the Development Battalion less than 5 days. Three of these came originally from the 7th Regiment, and 1 from the 3rd Regiment. They were transferred into

TABLE IV

WEEKLY "INFLUENZA" INCIDENCE RATE PER 1000 IN MAIN WHITE ORGANIZATIONS

ORGANIZATIONS	WEEK OF SEPT. 13-20	WEEK OF SEPT. 21-27	WEEK OF SEPT. 28-OCT. 4	WEEK OF OCT. 5-11	WEEK OF OCT. 12-18	TOTAL PERIOD OF EPIDEMIC
2nd E. T. R.	5.4	25.9	44.6	12.9	0.0	90.5
3rd E. T R	30.0	167.7	49.3	16.9	4.4	286.
4th E. T. R.	0.0	17.6	34.2	29.7	0.8	74.
5th E. T. R.	4.0	76.5	49.7	21.5	5.1	160.
6th E. T. R.	3.3	4.2	0.0	5.2	27.4	25.4
7th E. T. R.	0.2	2.4	240.3*	47.4	4.5	267.
E. O. T. S	1.5	0.7	11.6	41.0	26.2	87.7
All whites in Camp	5.8	41.9	94.9	28.1	6.8	177.0

*Over 30 per cent of this organization were limited service men who arrived at the camp about the 1st of September.

TABLE V

STRENGTH OF COMMAND OF SAPPER REGIMENTS AND WHITE DEVELOPMENT BATTALION. NUMBER OF CASES OF "INFLUENZA," AND CASE RATE PER 1000. OCTOBER 1 TO 18, 1918

ORGANIZATION	STRENGTH	NUMBER OF CASES OF INFLUENZA			TOTAL	RATE PER 1000
		Sept. 28-Oct. 4	Oct. 5-Oct. 11	Oct. 12-Oct. 18		
215th	582	19	34	1	54	93.
216th	216	10	3	4	17	78.7
217th	600	113	30	4	147	244.6
218th	642	95	35	4	134	208.2
219th	583	60	48	4	112	192.5
220th	549	45	28	2	75	136.3
Development Battalion No. 1	450	5	6	2	13	28.9

TABLE VI

AVERAGE WEEKLY STRENGTH OF COMMAND FOR MAIN WHITE ORGANIZATIONS FOR PERIOD OF EPIDEMIC

ORGANIZATION	WEEK OF SEPT. 13-20	WEEK OF SEPT. 21-27	WEEK OF SEPT. 28-OCT. 4	WEEK OF OCT. 5-11	WEEK OF OCT. 12-18	AVERAGE FOR PERIOD OF ENTIRE EPIDEMIC
2nd E. T. R.	3158	3085	2718	2791	2348	2820
3rd E. T. R.	2992	2690	3504	2840	1376	2680
4th E. T. R.	2395	1814	1113	1091	1031	1489
5th E. T. R.	4236	3817	3198	3115	2767	3425
6th E. T. R.	985	896	627	388	255	630
7th E. T. R.	6276	6116	4518	3569	3766	4849
E. O. T. S.	1339	1469	1639	1732	1754	1587
All Whites in Camp	22393	21400	20848	22196	19597	21287

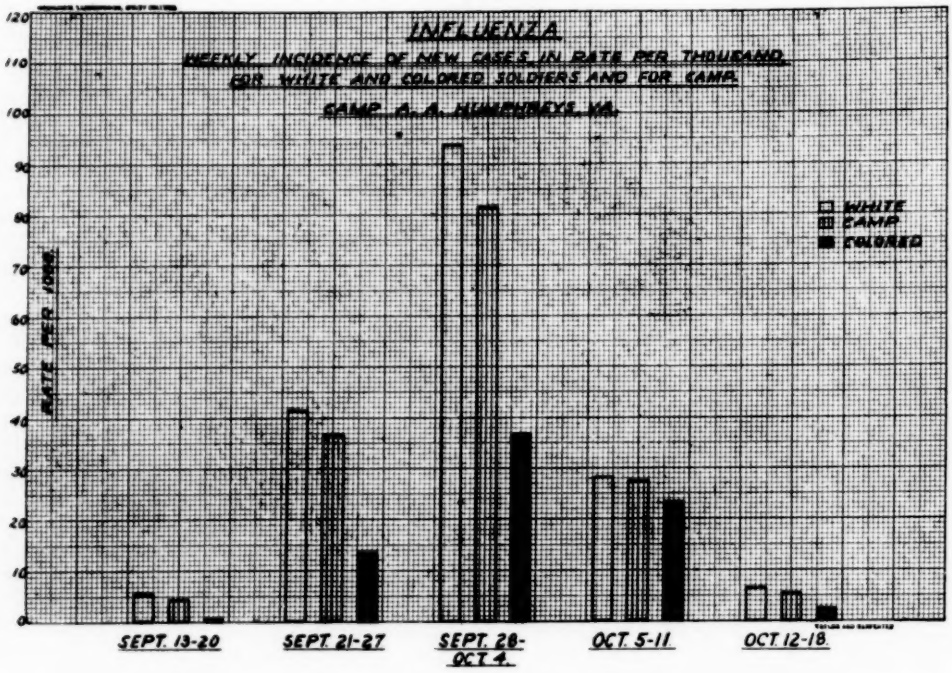
the battalion on the 27th and 28th of September, at a time when there was considerable "influenza" in both of these regiments and incidence was rising. That these cases brought the "influenza" with them can not be questioned. The first cases appeared in this organization on October 2 and 3, on which days there

were 6 cases. All of the 4 cases recently transferred appear on the infirmary record of this date. The 3 from the 7th Regiment developed exactly 4 days from the time they joined the organization. The other man from the 3rd Regiment was taken sick within 5 days after his transfer. All other men who were taken with "influenza" had been in the battalion at least 10 days.

Table IV shows the incidence rate per thousand in the principal white organizations of the camp for the five-week period of the epidemic. This also shows the incidence of new cases by weeks.

Six sapper regiments were organized during the epidemic and were made up from men from various organizations about the camp. They are considered

CHART 4.



by themselves, and the incidence of the disease in these organizations is given in Table V. It is difficult to classify the data from these organizations as they undoubtedly brought the infection with them and they vary greatly in strength. The 216th Sapper Regiment, for instance, had 216 men, while some of the other organizations were much larger.

Table VI shows the average weekly strength of the command for the principal organizations of the camp, and the average strength for each organization in the camp. This is the data from which the rate tables have been constructed. In some of the regiments, for instance the 3rd and 5th, the infirmaries served other smaller organizations. In such cases the strength of those additional organizations and the number of sick are included in the regimental strength and their morbidity tables. In determining the rates and the

floor space in the barracks, these facts are kept in mind and are considered with the organization.

Table VII deals with the actual number of cases each week in the white organizations and accounts for 3,771 of the cases in the camp. This table shows that the maximum for the 3rd and 5th Regiments occurred in the 2nd week, and for the 2nd, 4th and 7th Regiments in the 3rd week, the maximum for the Engineer Officers' Training School occurring in the 4th week, and the 6th Regiment in the 5th week of the epidemic.

INCIDENCE OF "INFLUENZA" IN COLORED ORGANIZATIONS

Chart 4 shows the weekly incidence of new cases in rate per thousand, for the white and colored troops. The data for this chart appear in Table IX. This chart is extremely interesting in view of the fact that it is generally considered that the colored race is far more susceptible to diseases of the respiratory tract than is the white race. The results of this epidemic show the exact reverse. The colored troops show a decidedly lower rate than the white troops all during the epidemic. The total rate is much lower and the weekly totals are also lower.

TABLE VII

WEEKLY NUMBER OF NEW CASES OF "INFLUENZA" IN MAIN WHITE ORGANIZATIONS FOR PERIOD OF EPIDEMIC

ORGANIZATION	WEEK OF SEPT. 13-20	WEEK OF SEPT. 21-27	WEEK OF SEPT. 28-OCT. 4	WEEK OF OCT. 5-11	WEEK OF OCT. 12-18	TOTAL PERIOD OF EPIDEMIC
2nd E. T. R.	17	80	122	36	0	255
3rd E. T. R.	90	451	173	46	6	766
4th E. T. R.	0	32	38	31	9	110
5th E. T. R.	17	293	159	67	14	550
6th E. T. R.	3	4	0	2	7	16
7th E. T. R.	1	15	1089	169	17	1291
E. O. T. S.	2	1	19	71	46	139
Development Battalion			5	6	2	13
All Whites* in Camp	130	893	1978	632	133	3771

*Includes other small organizations not mentioned in Table.

Table VIII gives rates for the colored organizations.

TABLE VIII

INCIDENCE OF "INFLUENZA" IN COLORED ORGANIZATIONS FOR PERIOD OF EPIDEMIC. SEPTEMBER 13 TO OCTOBER 18, 1918

ORGANIZATION	AVERAGE STRENGTH OF COMMAND	TOTAL CASES	CASE RATE PER 1000
Casual Detachment	1487	147	99.
540th Service Bn.	916	85	92.8
547th Service Bn.	1002	129	129.
548th Service Bn.	894	80	89.6
549th Service Bn.	301	13	43.2
550th Service Bn.	628	8	12.7
42nd Separate Co.	250	4	16.0

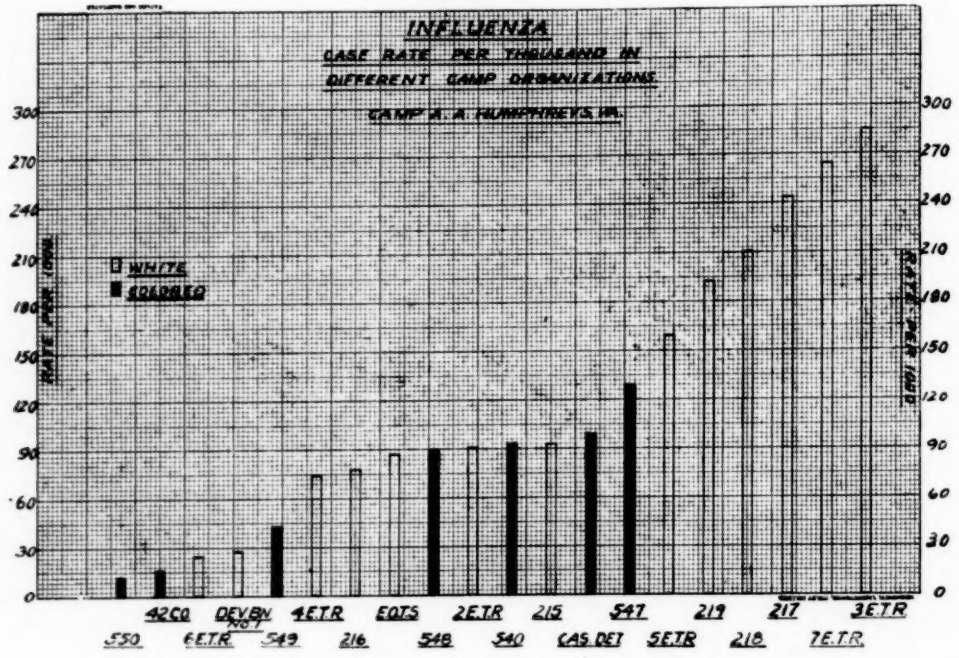
TABLE IX

WEEKLY INCIDENCE OF NEW CASES OF "INFLUENZA" IN WHITE AND COLORED TROOPS. RATE PER 1000

RACE	ENTIRE PERIOD	WEEK OF SEPT. 13-20	WEEK OF SEPT. 21-27	WEEK OF SEPT. 28-OCT. 4	WEEK OF OCT. 4-11	WEEK OF OCT. 12-18
White	177.0	5.8	41.9	94.9	28.1	6.8
Colored	76.0	0.6	13.7	36.8	23.4	2.8
Entire Camp	154.1	4.6	36.7	81.4	27.4	5.8

Chart 5 shows the rate per thousand for the different organizations in the camp. It varies a little from the data shown in Chart 4, in that certain of the

CHART 5.



colored organizations are higher than some of the white organizations. However, the chart coincides with the data shown on Chart 4. The highest rate in the colored organizations, the 547th Service Battalion, is far less than the rate in the 5th, 7th or 3rd Regiments, and only slightly in excess of the incidence in the Engineer Officers' Training School and the 4th Regiment. A very interesting comparison in this chart is between the 42nd Company, which is colored, and the Engineer Officers' Training School and the 6th Regiment. These organizations are all quartered in the same area. They are under practically the same discipline and the same medical treatment. There can be, therefore, very little error regarding the diagnosis and difference in methods of living and diet received by these men. The 42nd Company shows the lowest rate in the entire camp, excepting the 550th Service Battalion. The comparison between the 550th Bat-

talion and the 42nd Company is not exactly just, because the 550th Battalion was just organized and did not exist in the early days of the epidemic.

Table IX shows in tabulated form the same data as appeared on Chart 4. Here we see that the rate among the colored troops is much lower than the rate among the white troops until next to the last week when they approached the white organizations closely. The entire period shows a difference in rate of something over 101 per thousand. This means that the incidence among colored troops was only 43 per cent of that among whites. These considerations call for a revision of our opinions as to the susceptibility of the colored race to diseases of the respiratory tract. There were 7 colored organizations in the camp during a considerable part of the epidemic; the rate varies considerably in these. We have already discussed the low rate in the 42nd Company which apparently is due to careful prophylaxis, including larger floor space and the use of cubicles. The 547th Service Battalion shows the highest rate among colored troops. This Battalion was divided into two parts, one part living about seven miles from the camp on the Telegraph Road doing road work. Through an oversight this organization was for a considerable time without medical attention. It had become thoroughly infected before any systematic measures of prevention were instituted and I believe this fact has to do with the large rate in that organization. Three of the Battalions have almost identical rates and the 549th and 550th Battalions with their low rates are probably due to the fact that these organizations were not organized at the beginning of the epidemic and the large number of men who developed the disease in the beginning were credited to the organization to which they were attached.

HOUSING

The general difference between the white and colored troops in this camp is in their housing. All the white troops are now housed and have been for some time in cantonment buildings which allow on the average 50 square feet of floor space per man. The colored troops, on the other hand, with the exception of the 42nd Company, are housed in tents. At the beginning of the epidemic there were six men in a tent, but later the number was reduced to five. It would seem but natural that life in a tent in the summer months, with better ventilation and more time in the open air, would cause a lower rate than where men are housed in barracks that are not as well ventilated. The experience of living in tents, however, does not make one believe that the ventilation is particularly good in tents. The 42nd Company was housed under exactly the same conditions as are the white troops of the Engineer Officers' Training School and the 6th Regiment. It would therefore seem to indicate that the colored race when living under good hygienic conditions is not as susceptible to "influenza" as the white race under the same conditions.

Chart 6 shows in black the "influenza" rate in the principal white organizations in the camp. This chart is based on the data in Table X. In white is shown the floor space allowed each man in each organization. It is not proper or just to attribute the differences shown here alone to the amount of floor

CHART 6.

INFLUENZA

RELATION BETWEEN FLOOR SPACE PER PERSON AND INCIDENCE RATE PER THOUSAND IN DIFFERENT CAMP ORGANIZATIONS.

CAMP A. A. HUMPHREYS, VA.
1918.

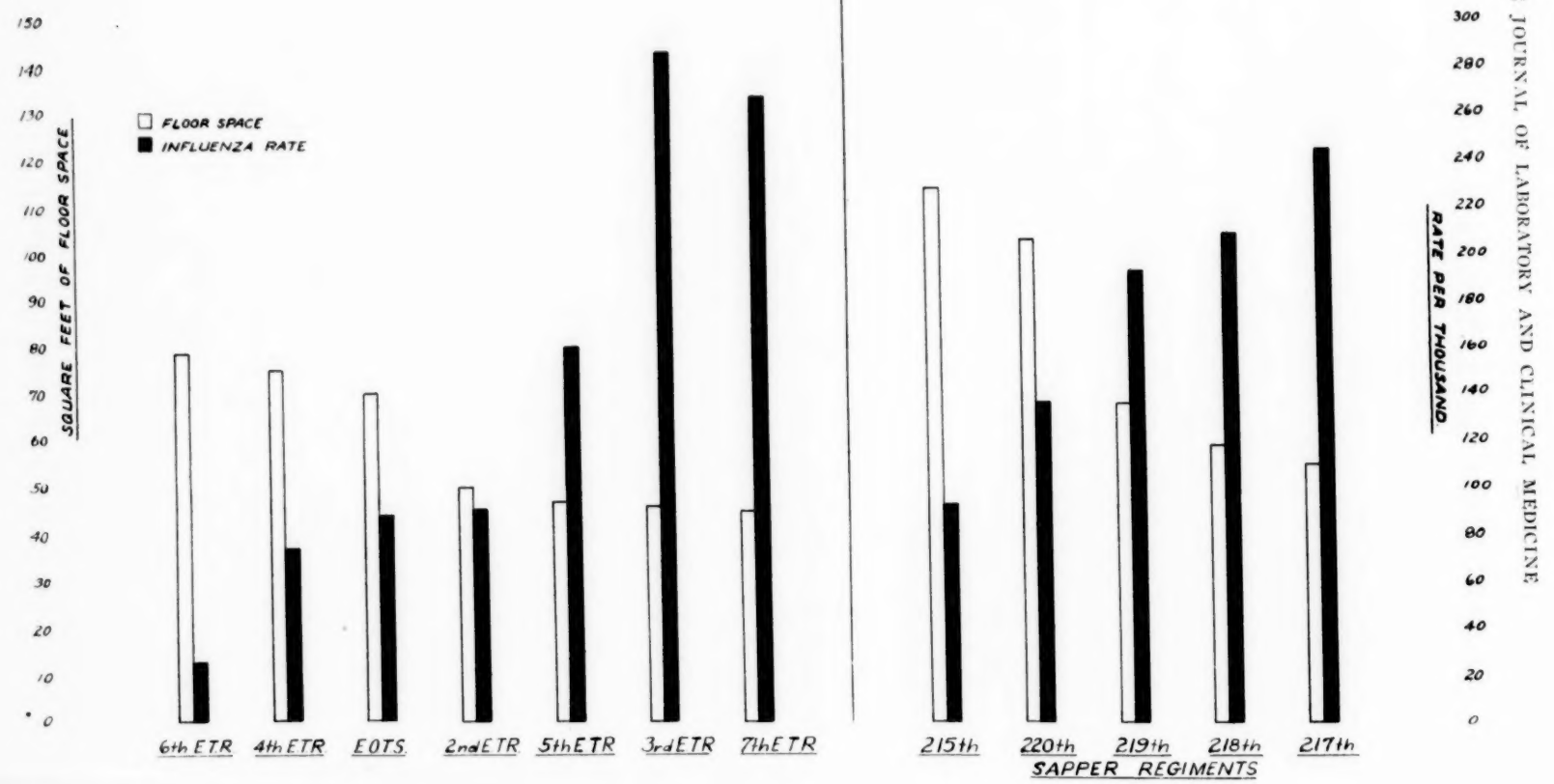


TABLE X

NUMBER OF PERSONS PER BARRACKS BY DIFFERENT ORGANIZATIONS. SQUARE FEET OF FLOOR SPACE PER PERSON, AND "INFLUENZA" RATE PER 1000

ORGANIZATION	NUMBER OF BARRACKS	NUMBER OF MEN PER BARRACKS	NUMBER OF SQUARE FEET OF FLOOR SPACE	INFLUENZA RATE PER 1000
6th Regiment	15	42	78.5	25.4
4th Regiment	34	44	75.	74.
E. O. T. S.	34	47	70.	87.7
2nd Regiment	43	66	50.	90.5
5th Regiment	49	70	47.	160.
3rd Regiment	42	72	46.	286.
7th Regiment	52	73	45.	267.
		"SAPPER REGIMENTS" (NEWLY FORMED)		
215th	17	29	114.	93.
220th	17	32	103.	136.3
219th	12	49	68.	192.5
218th	12	56	59.	208.2
217th	10	60	55.	244.6

space allowed each organization, but it certainly points very strongly to the fact that the incidence of the disease varied with the density of the population, although not with mathematical regularity. These figures are not mathematically accurate, as it was impossible at the time the table was constructed to get the exact figures as to the number of men that occupied each barracks during the epidemic. It was therefore necessary to average the conditions found in each organization. The least incidence appeared in the 6th and 4th Regiments and the Engineer Officers' Training School. In addition to the increased floor space, these regiments had for a long time been provided with curtains hanging between the individual beds in the barracks, thus making a cubicle for each man. Without doubt this largely reduced the incidence of infection in these regiments. However, the floor space does have a very important bearing on the case, because during the day these curtains are quite frequently rolled up and where large numbers of men are crowded in a barracks they naturally come into very close contact with each other during the hours they are not on the drill field. It might be said that during the epidemic every endeavor was made to keep the men in the open air as much as possible.

Considering the cases further, we find there is very little difference between the floor space in the 2nd and 5th Regiments, and yet there is a large difference between the rates for these regiments. This same apparently disproportionate difference in rates may be said to exist for the 5th, 3rd and 7th Regiments. As mentioned before, other factors help to account for these differences. However, in considering the 7th Regiment and the 5th Regiment it is to be remembered that these regiments contain many men who have been in the service but a short time and the 7th Regiment contains about 2,000 men physically more or less unfit for the service. The 3rd Regiment was early infected and many of the men came down before our plan of combat was fully developed, which no doubt accounts for the great number of cases in that Regiment. It may also be

said that during a considerable part of the epidemic there was not the same amount of activity among the medical officers of the 3rd Regiment as in some of the other regiments.

DISH WASHING AND "INFLUENZA"

It has been suggested that the disease is spread through the mess pans and other dishes. That there is some ground for this belief is not denied. The washing of dishes in the company mess halls has never been satisfactory and early in the epidemic efforts were made to improve conditions, resulting in an attempt to sterilize being made by most of the organizations. However, a study of the disease in the 2nd and 3rd Regiments with the question in mind, does not convince one that the dishes were responsible for the spread of the disease in this camp.

COMPLICATIONS OF "INFLUENZA" WITH PNEUMONIA

"Influenza," uncomplicated, is not a cause of death. The records here show four deaths from "influenza." I am of the opinion that the causes were really bronchopneumonia that could not be recognized by our methods of diagnosis.

Of the 4,237 cases of "influenza" considered in this report, 1171 developed pneumonia of one form or another, a percentage of 27.6. Of the pneumonia cases, 94 were lobar with 23 deaths, a percentage of 24.5; 1077 were broncho with 390 deaths, a percentage of 36.2. The mortality from all cases was 35.2 per cent.

Table XI shows the number of cases of pneumonia and the deaths by weeks.

TABLE XI

NUMBER OF CASES OF PNEUMONIA AND DEATHS FROM PNEUMONIA

WEEK OF	LOBAR PNEUMONIA		BRONCHO PNEUMONIA		TOTAL	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
September 13-20	13	3	14	0	27	3
September 21-27	11	3	75	6	86	9
September 28-Oct. 4	40	6	423	81	463	87
October 5-11	24	6	470	207	494	213
October 12-18	4	5	73	79	77	84
October 19-25	2	0	22	17	24	17
Total Period of Epidemic	94	23	1077	390	1171	413

TABLE XII

WEEKLY DEATH RATE PER 1000 FOR PNEUMONIA FOR PERIOD OF "INFLUENZA" EPIDEMIC

WEEK OF	STRENGTH OF CAMP COMMAND	NUMBER OF CASES OF PNEUMONIA	NUMBER OF DEATHS FROM PNEUMONIA	DEATH RATE PER 1000 FROM PNEUMONIA
September 13-20	29210	27	3	0.13
September 21-27	26230	86	9	0.34
September 28-Oct. 4	27136	463	87	3.21
October 5-11	28518	494	213	7.48
October 12-18	26053	77	84	3.22
October 19-25	22688	24	17	0.75
Total Period	26637	1171	413	15.5

TABLE XIII

PNEUMONIA CASES AND INCIDENCE PER 1000, BY CAMP ORGANIZATIONS
SEPT. 13 TO OCT. 25, 1918

(WHITE)

ORGANIZATION	STRENGTH OF COMMAND SEPT. 13 TO OCT. 18	NUMBER OF CASES OF PNEUMONIA		TOTAL	INCIDENCE RATE PER 1000	TOTAL, "INFLUENZA" CASES	PER CENT OF "INFLUENZA" CASES TREATED IN HOSPITAL	RATIO BETWEEN PNEUMONIA AND "INFLUENZA" CASES
		LOBAR	BRONCHO					
2nd E. T. R.	2820	8	50	58	20.6	255	39.3%	1:4.4
3rd E. T. R.	2680	17	112	129	48.2	766	39.1	1:5.9
4th E. T. R.	1489	2	28	30	20.2	110	45.5	1:3.7
5th E. T. R.	3425	13	132	145	42.4	550	34.4	1:4.2
6th E. T. R.	630	0	9	9	14.3	16	94.0	1:1.6
7th E. T. R.	4849	20	314	334	69.0	1291	24.8	1:3.9
E. O. T. S.	1587	3	53	56	35.2	139	68.0	1:2.5
215th Sapper Regt.	582	0	15	15	25.8	54	31.5	1:3.6
216th Sapper Regt.	216	0	9	9	41.6	17	17.6	1:1.8
217th Sapper Regt.	600	0	23	23	38.3	147	16.3	1:6.4
218th Sapper Regt.	642	1	14	15	23.4	134	24.6	1:8.5
219th Sapper Regt.	583	0	24	24	41.2	112	21.6	1:4.7
220th Sapper Regt.	549	1	11	12	21.8	75	30.7	1:6.2
1st Development Bn.	450	1	11	12	26.7	13	100.0	1:1.8
Miscellaneous White Organizations		4	32	36				
TOTAL WHITE	21287	70	837	907	42.6	3771	34.9	1:4.2
(COLORED)								
Casual Detachment	1487	7	55	62	41.7	147	71.5	1:2.4
540th Service Battalion	916	3	41	44	48.1	85	53.0	1:1.9
547th Service Battalion	1002	5	73	78	78.	129	62.8	1:1.7
548th Service Battalion	894	4	28	32	35.8	80	42.6	1:2.5
549th Service Battalion	301	0	7	7	23.3	13	69.2	1:1.9
550th Service Battalion	628	0	8	8	12.7	8	100.0	1:1.0
Miscellaneous Colored Organizations		3	30	33		4		
TOTAL, COLORED	6143	22	242	264	43.0	466	62.	1:1.8
TOTAL, CAMP	27430	92	1079	1171	42.7	4237	38.%	1:3.6

CHART 7.

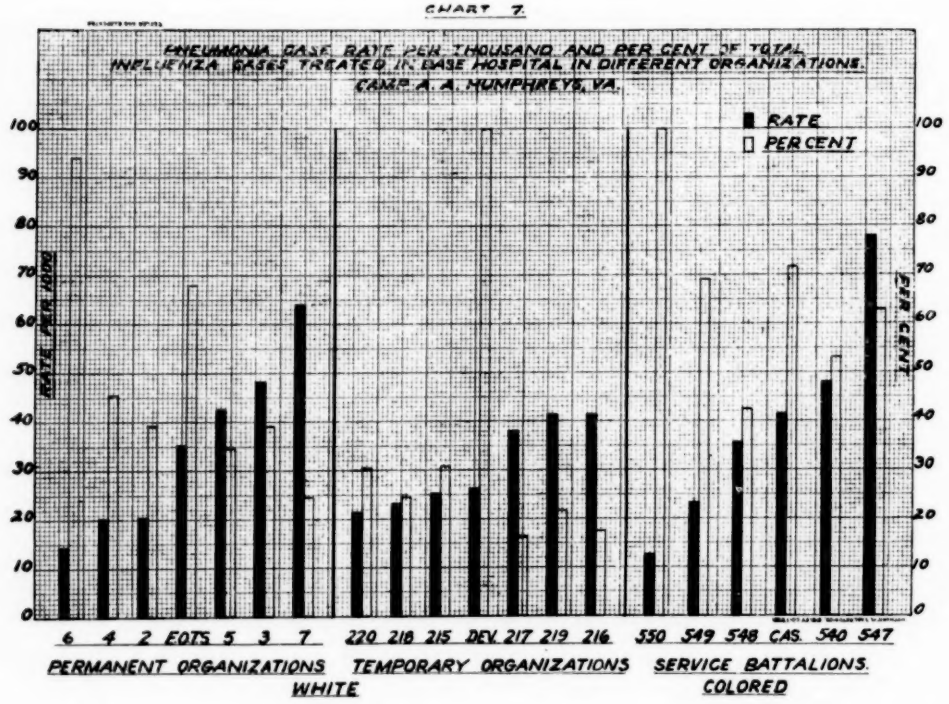


Table XII shows the deaths from pneumonia by weeks, and the total death rate from the complication.

Pneumonia is always more fatal among the colored race, but in view of the low incidence of "influenza" among the colored troops it was expected that pneumonia would show a correspondingly low rate. A study of the incidence of pneumonia in all the organizations of the camp was made and is shown in Table XIII. In it are columns showing the percentage of cases of "influenza" treated in the hospital, and the ratio between pneumonia and "influenza."

Among the white troops the incidence of pneumonia appears to vary with the density of population. This table shows also that the incidence of pneumonia is much higher among the colored troops although the percentage of cases of influenza in the hospital was much greater.

The relation between hospitalization and incidence of pneumonia brought out in a recent paper, is not apparent here. The 6th Regiment, with a low incidence of "influenza" and with 94 per cent of the cases treated in the hospital, shows a ratio between pneumonia and "influenza" of 1 to 1.6. The same is shown in the colored organizations.

I, however, do not take issue on the question, because it is difficult to disentangle the various factors which produce the conditions observed in this epidemic. A factor that played a big part in this camp was the high morale of the men, which made them attempt to fight the disease. Many such cases developed pneumonia, especially in the Engineer Officers' Training Camp and the 6th Regiment.

The relation between pneumonia and hospitalization is shown on Chart 7.

CONCLUSIONS

The result of this study seems to indicate:

1. That the incidence of the disease increases with the density of population in barracks.

2. That the hanging of a sheet between the individual beds in the barracks was of value in preventing infection.

3. That the negro race suffered much less from the disease than did the white.

4. That there were more cases complicated with pneumonia among the colored troops and that the disease was more fatal among them.

The charts and statistical data were compiled under my direction by Sergeant Joseph Herzstein, Medical Department.

APPENDIX

A

ARTICLE IN CAMP NEWSPAPER "THE CASTLE," SEPT. 8, 1918

We have heard a great deal recently regarding the so-called "Spanish Influenza." Influenza is a disease that has been known in this country for about 100 years. Every once in a while it becomes epidemic and spreads all over the country. One of the most noted epidemics this country has ever had was in 1889 and 1890. It is more prevalent in the winter months, although not unknown in the fall and spring months. In itself influenza is not particularly serious. It, however, so reduces the resistance of the person that not infrequently he becomes the victim of other diseases such as pneumonia and tuberculosis. The mortality from influenza is usually due to one of those diseases, or to diseases of the heart which may accidentally be associated with influenza. At the present time influenza is becoming very prevalent in the United States. Recent reports from some of the camps show that several thousand cases of this disease developed within one or two weeks.

Influenza is a communicable disease and is transmitted from one person to another through the medium of the fine spray thrown out from the nose or throat during coughing or spitting. It can easily be controlled. It does not depend upon the weather nor upon dampness. It is more common in the winter time because at that season persons are more likely to congregate in badly ventilated rooms and come in closer contact with their fellows.

The prevention of the disease is simple and consists of avoiding the disgusting habit of coughing into another's face. It is very probable that this camp may during the coming fall or winter be visited by an epidemic of this disease. We will be able to control it if every man in the camp will do his part. His part will not require any work or hardship. It simply means that the individual must hold before his mouth and nose each time he coughs, a handkerchief or a piece of newspaper. In case paper is used it should always be burnt as soon as possible. Men should also avoid spitting on the floor or coughing in the air.

Do your part to prevent this disease and by so doing help keep Camp Humphreys "First in Health!"

B

War Department
Headquarters, Camp A. A. Humphreys,
Virginia.

September 18, 1918.

Memorandum No. 399.

1. During the past winter the principal diseases encountered by the American troops in camps in the United States, were diseases spread through the excretions of the respiratory tract, including the mouth. These diseases include: Pneumonia, Influenza, Bronchitis, Cerebrospinal Meningitis, Measles, and Scarlet Fever. Without doubt there are carriers of all these diseases in the different organizations of this camp. At the present

time we are unable to discover these men. It is therefore necessary to take precautions as far as possible to limit the spread of these diseases, and the following instructions will be complied with:

2. On the left side of each bed in the barracks a shelter half will be hung. This can be readily accomplished by placing a long stick at the head, and a short stick at the foot of the bed. This arrangement of the beds will greatly diminish the chances of infection.

3. All the enlisted men of the camp will attend a lecture on the spread of these diseases, on the following schedule:

Wednesday	at 5 P.M.	The entire 7th Regiment.
"	" 7 P.M.	The entire 5th Regiment.
Thursday	" 5 P.M.	The entire 4th Regiment.
"	" 7 P.M.	The entire 2nd Regiment.
Friday	" 5 P.M.	The Officers' Training Class.
"	" 7 P.M.	The entire 3rd Regiment.
"	" 8 P.M.	The entire Service Battalions, including Casual Camp and Sanitary Bns.

4. One officer must accompany each organization.

By command of Brigadier General Kutz:

John E. Harris,
Major, C. E.
Adjutant

C

War Department
Headquarters, Camp A. A. Humphreys,
Virginia.

September 27, 1918.

Memorandum No. 436.

Regimental Commanders, Battalion Commanders, and Commanding Officers of Detachments will see to it that Company Commanders personally supervise the falling out of all men at Reveille and Retreat formations who appear to have colds. These possible cases will be specifically called for and sent to Regimental Surgeon to determine whether or not they have Spanish influenza.

By command of Brigadier General Kutz:

George Mayo,
Major, C.E.
Actg. Adjutant.

D

Office of Camp Surgeon
Camp A. A. Humphreys, Va.

September 30, 1918.

Memorandum to All Regimental and Battalion Surgeons and Surgeons of the Base Hospital:

1. The Surgeon General directs that during the present emergency all cases of infectious diseases, including influenza and colds, be so arranged in wards that each man shall have 100 square feet of floor space. If the wards now assigned to you are not sufficient for this purpose, make requisition on the Commanding Officer of your unit for additional space.

2. As it is difficult to determine whether men with coryza are coming down with influenza or not, you are directed to, as far as possible, have all men with colds report to the Infirmary twice a day, and instill into the nostrils of each man two drops of a 10 per cent solution of Argyrol or similar silver salt.

E

War Department
Headquarters, Camp A. A. Humphreys,
Virginia.

Sept. 30, 1918.

Memorandum No. 449.

Organizations will draw six (6) feet of sheeting from the Quartermaster for each member of organization. This is for the purpose of constructing screens to be placed between cots as directed by the Surgeon. Organizations will supply all other material themselves. Installation will be completed as soon as possible.

By command of Brigadier General Kutz:

George Mayo,
Major, C.E.
Actg. Adjutant.

F

War Department
Headquarters Camp A. A. Humphreys,
Virginia.

October 3rd, 1918.

General Order No. 15

1. In view of the serious epidemic of Spanish influenza at this camp and upon the recommendation of a special investigating officer from the office of the Surgeon General, the following precautions will be strictly observed in all organizations.

No more than five occupants to a pyramidal tent will be permitted. All windows in barracks will be kept open full width from Reveille to Retreat. All except those on the windward side will be kept open from Retreat to Taps, and from Taps to Reveille all windows will be kept at least one-half way open. Compliance is again directed to Memorandum No. 399, which states that shelter halves will be stretched on one side of each cot for its full length. This practice has not been fully carried out in some of the regiments. Company commanders will be responsible for the inspection of barracks by an officer between Taps and Midnight, and will submit with their morning report a written statement of conditions found in each building at time of inspection. Further, the Officer of the Day or the Officer of the Guard will make an inspection of barracks between Midnight and Reveille, and submit a written report, with the guard book, of conditions found in each building at time of inspection. Regimental commanders will require reports each day regarding the enforcement of these regulations by the officers responsible for the inspections.

2. It has been noticed, lately, that fly-paper is not used in some of the Messes in this camp, and as a consequence, there are a large number of flies in their messes. Strenuous efforts will be made to reduce the number of flies.

3. Methods of washing dishes in most Messes are not such as to insure adequate cleanliness and sterilization. Steps will be taken after each meal so that all dishes will pass through boiling water.

4. Where barracks are used exclusively for the care of the sick, means will be taken of providing these Messes with a suitable light diet.

5. Every effort will be made to reduce the use of common drinking cups.

6. Efforts will be made to prevent the men from congregating in crowds, particularly indoors. In all exchanges of this camp steps will be taken to post men at the entrance so as to prevent crowding and in the general assembly halls only enough men will be admitted so that not more than every other seat will be occupied.

By command of Brigadier General Kutz:

George Mayo,
Major, Engineers,
Acting Adjutant.

G

Office of Camp Surgeon,
Camp A. A. Humphreys, Va.,

October 4, 1918.

Memorandum to All Medical Officers:

1. The Surgeon General directs that all the men who have suffered from influenza be kept off duty for at least ten days after their temperature has reached normal. This, however, does not mean that the men need remain in the Base Hospital. They may be carried in quarters, but kept at rest and under good care during these ten days. The object of this is to cut down instances of pneumonia following influenza.

2. The inspection made on October 3rd by Colonel Chamberlain, M.C., showed the following defects, which should be remedied immediately:

(a) Not all the patients were in cubicles.

(b) There were a great many flies in kitchens and in buildings where patients with influenza were being treated.

(c) In not a few instances men had expectorated on the floor. Colonel Chamberlain suggested that a newspaper be placed on the floor near the bed, and spit cup placed on it. The whole should be burned at frequent intervals during the day. Newspapers are plentiful in the camp and there should be no difficulty in getting them.

(d) The condition of the floors of some of the buildings was not satisfactory, being littered with dirt and in some cases unconsumed food. All floors should be swept several times a day with damp sawdust, which should be later burned. Special attention should be paid to keeping floors clean and to prevent remnants of food from being thrown about the buildings.

(e) In some cases it was found that men were receiving food which was not satisfactory. In most of the companies the mess fund is in excess of the amount allowed by camp orders, and therefore there should be no difficulty in making whatever extra purchases are necessary in order to properly subsist the sick in the camp. These surgeons should pay particular attention to this. Where the medical detachment is running a mess you can not call upon the company for additional subsistence under these circumstances.

3. If there are not sufficient line men detailed for duty in the wards, make requisition to the Regimental Commander for the number needed.

4. The Surgeon General has directed that all patients transferred to the Base Hospital by ambulance be masked. Until such time as we are able to obtain a sufficient supply of masks from the Red Cross, you are directed to make handkerchief masks from cheese cloth. These masks are not to be destroyed when once used, but are to be returned to the infirmary and washed with soap and water and sterilized.

I. W. Brewer,
Lt. Col. M.C.
Camp Surgeon.

H

War Department
Headquarters, Camp A. A. Humphreys,
Virginia.

October 8, 1918.

Memorandum No. 485.

1. No more than five men will be allowed to occupy a pyramidal tent. The number of men in Barracks will not exceed the authorized number for each building. Standard Barracks in this camp provide accommodations for 66 men, at the rate of 50 sq. ft. of floor space for each man. This number will not be exceeded. All barracks will be aired each day by opening all the windows. At night at least one-half of all the windows will be kept open. Tents will be furled on every sunny day. The ventilators at the top of tents will be kept open. Where tin hoods are provided for ventilation, they will be arranged so as to leave 2 inches between the bottom of the canvas and the tin hood. During the present epidemic all bedding will be aired and sunned daily. Cubicles in accordance with previous orders will be provided for every man, whether in tents or in barracks. Sheeting for this purpose can be procured from the Quartermaster.

2. In sweeping the Barracks every effort will be made to diminish the amount of dust. There is a large amount of clean sawdust in the camp. It should be procured and placed in a dry place and dampened and used for sweeping. This will practically eliminate all dust.

3. Special attention will be paid to flies. Fly paper, fly traps, and swatters will be used. If the Quartermaster has not a sufficient number of fly traps they can be easily improvised from plans which can be obtained from the secretary of the Schools. Swatters can be easily made from waste screening.

4. Commanding Officers of organizations will see that mess utensils are thoroughly sterilized after being used. Where enamelware is provided it should be collected in tubs and boiled. Where individual mess kits are used an abundance of very hot water should be provided. It has been noticed in a large number of cases that water for washing dishes has been practically stone cold and very dirty before the last men have washed their dishes.

5. The officer present at the mess will, before each meal, caution all men of the danger of coughing while at meals. Men who cough will be sent from the mess hall and required to eat their meals by themselves at a later time.

6. At least 4 noncommissioned officers will be detailed for duty at each Y. M. C. A. building each evening. They will report one-half hour before each entertainment and remain until the entertainment is over. Their duties will be to enforce the regulations regarding coughing and crowding. Men who cough will be excluded from buildings, unless they are using proper precautions. Not more than every other seat in the building will be occupied, in both directions. In other words, no man will sit in close proximity to another. Exchange officers will see that no more men are allowed to enter the exchange at one time than may stand at the various counters. Crowding of men around the counters will thus be prevented.

7. Every effort will be made to keep the men out of doors during the entire day. They will be given such drill and other instructions as may be necessary. Company Commanders will, however, avoid strenuous exercise, as at this time it is not wise to have the men become tired or overheated.

In the sections where hot water is not provided in the bath houses, arrangements will be made with the Commanding Officer in adjacent areas for use of the bathing facilities there at specified times. Every man should have a bath at least once a week, and twice a week if possible.

8. Company Commanders will report immediately to the surgeon any man who apparently is sick. Sick men will not be kept in the same quarters with the well, unless the surgeon certifies that illness is of a nature that will not be transmitted. All officers who are sick will immediately report to the surgeon for examination. Surgeons will send to the Base Hospital all officers suffering from symptoms of influenza. The noncommissioned officer in charge of Barracks will see that the regulations regarding spitting in and about the Barracks are carefully observed.

By command of Brigadier General Kutz:

George Mayo,
Major, C.E.
Acting Adjutant.

THE SALICYLATES. X. THE SPECIFICITY OF SALICYLATE IN RHEUMATIC FEVER*

By Paul J. Hanzlik, M.D.; R. W. Scott, M.D.; and P. C. Gauchat, M.D.
Cleveland, Ohio

ASIDE from the striking symptomatic relief, the claim for the specificity of salicylates in rheumatic fever lacks scientific evidence. Some of the theories for the alleged specificity have been recently tested and found wanting.[1] The reported beneficial effects of other procedures, such as the foreign protein therapy of J. L. Miller,[2] rest, and others in the treatment of rheumatic fever tend to weaken rather than support the arguments for specificity both as to etiology and symptomatic relief. Owing to the uncertainty of the etiology of rheumatic fever it is manifestly impossible to investigate the specificity of salicylate with any satisfaction or convincing accuracy from this standpoint. This limits us practically to a study of the symptoms.

Essentially, the problem resolves itself into a comparison of the therapeutic effects of salicylate with other agents chemically different, but possessing similar pharmacologic actions. Two methods of approach may be utilized for this: 1. A statistical study of series of cases receiving the different forms of medication may be made. Such a study is very tedious and requires a large number of cases. It has the advantage that the elements of rest and natural recovery may be more satisfactorily controlled. 2. A careful study of the effects of both types, i. e., salicyl and nonsalicyl medication in the same individual should be able to yield equally important, interesting and conclusive results. This is not so time-consuming and requires a smaller number of individuals. However, the disadvantage of the elements of rest and natural recovery must be reckoned with in the terminal medication, and are not so easily eliminated. On the other hand, if recovery occurs without terminal medication, which in our series always consisted of salicylate, the argument against salicyl is conclusive. For the present, and because of convenience, we have used the individual experimental rather than the statistical method. All told, nine patients have been observed. Enough results have been obtained to justify a report of the progress of our work. Summarized protocols of all the patients are appended at the end of the paper.

METHOD

The patients were first treated with nonsalicyl medication, and if no relief was obtained within a reasonable period of time, as indicated by the progress of the condition, salicylate up to "toxicity" in the usual way was administered. That is, the antipyretic and analgesic properties of salicylate were imitated by combinations of other drugs such as morphine and quinine, which are chemically different from salicylate, but possess similar antipyretic and analgesic

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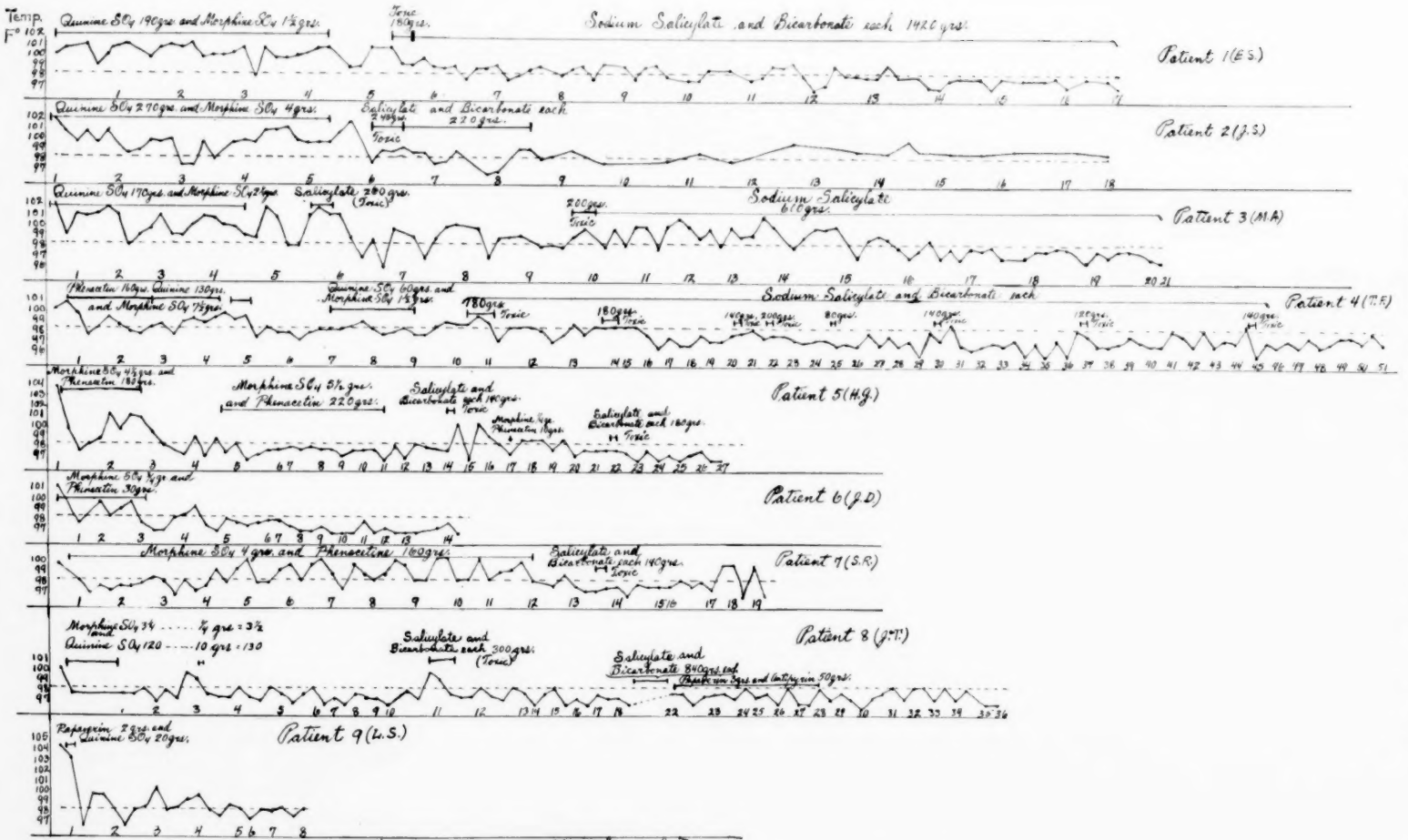
Temp. F°
Quinine SO4 190grs. and Morphine SO4 1½grs.
Sodium Salicylate and Bicarbonate each 1420 grs.
Patient 1 (E.S.)
Quinine SO4 270grs. and Morphine SO4 4grs.
Salicylate and Bicarbonate each 270grs.
Patient 2 (J.S.)
Quinine SO4 170grs. and Morphine SO4 2½grs.
Salicylate 200 grs. (Toxic)
Sodium Salicylate 610 grs.
Patient 3 (M.A.)
Phenacetin 140grs. Quinine 130grs. and Morphine SO4 7½grs.
Quinine SO4 60grs. and Morphine SO4 7½grs.
Sodium Salicylate and Bicarbonate each
Patient 4 (T.F.)
Morphine SO4 4½grs. and Phenacetin 180grs.
Morphine SO4 5½grs. and Phenacetin 220grs.
Salicylate and Bicarbonate each 140grs.
Patient 5 (H.G.)
Morphine SO4 ½gr. and Phenacetin 30grs.
Patient 6 (J.D.)
Morphine SO4 4grs. and Phenacetine 160grs.
Salicylate and Bicarbonate each 140grs.
Patient 7 (S.R.)
Morphine SO4 ¾ ..... ½gr. = 3½
Quinine SO4 120 ..... 10 grs. = 130
Salicylate and Bicarbonate each 300grs. (Toxic)
Salicylate and Bicarbonate 840grs. and
Patient 8 (J.T.)
Papaverin 2grs. and Quinine SO4 20grs.
Patient 9 (L.S.)
Number of Days

Fig. 1.—Effects of nonsalicyl and salicylate medication on the temperature in rheumatic individuals.

qualities. In this way, the symptoms could be readily combated, and if complete relief ensued without further medication, no specificity for salicylate, either etiologic or symptomatic, could be claimed. In addition, cathartic salts were frequently administered to avoid the constipating action of the opiates, for it was frequently observed that the maintenance of fever and constipation were associated, the patient otherwise being quite comfortable in many respects. "Complete relief" was judged by the prompt and permanent fall of body temperature

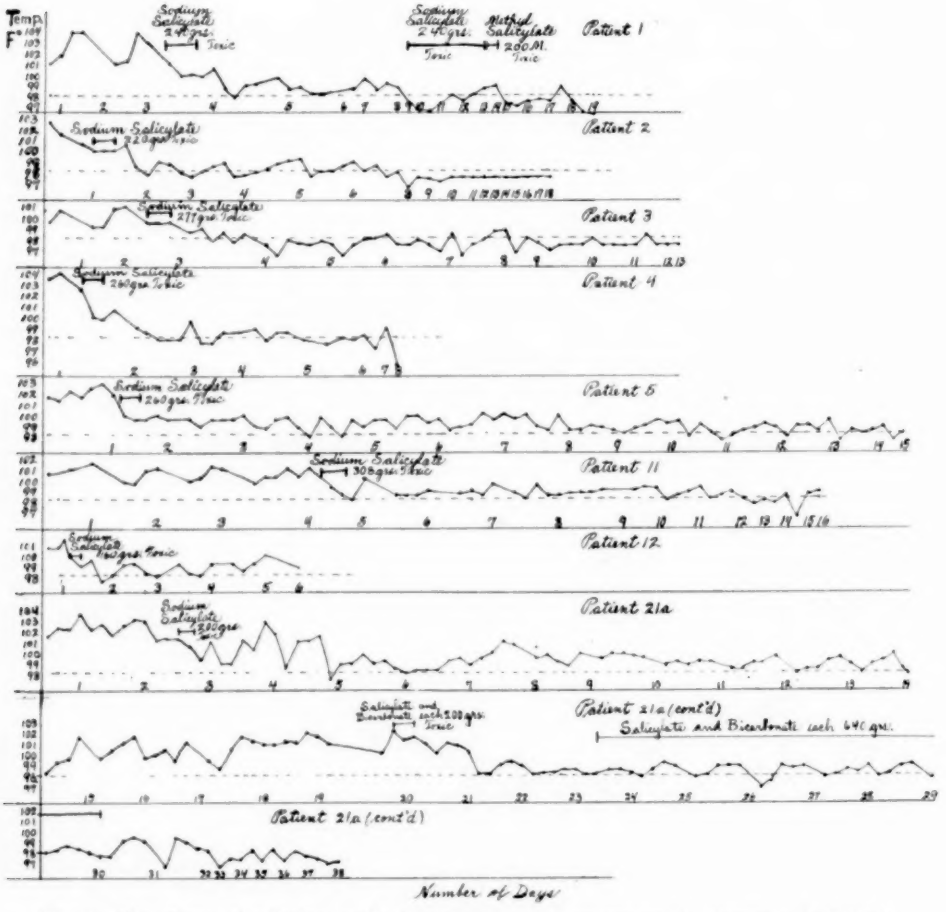

Fig. 2.—The effects of salicylate medication alone on the temperature in rheumatic individuals.

to normal, together with the disappearance of pain, redness, and swelling in the joints, and the restoration of general comfort. When only some of the symptoms were relieved, or all imperfectly, the relief was regarded as partial. When the symptoms persisted unabated, the result was called "no relief." On the whole, rather large doses, although variable, of opiates and the various antipyretics were used, and this is believed to be correct in principle, for it appears that the prompt relief generally obtained with salicylate is due to the marked effects of the very large doses used. Constriction of the pupil and slowing of the

respiration served as guides in the administration of the opiates, and changes in the pulse for the various antipyretics. Brief descriptions of the comparative effects of the two kinds of medication follow:

TEMPERATURE

This was promptly lowered in a majority [six, Patients 2 (J. S.), 4 (T. F.), 5 (H. G.), 6 (J. D.), 8 (J. T.), 9 (L. S.); Fig. 1] of all the patients by the nonsalicyl combinations, and also by salicylate (five patients, 1, 2, 3, 4, 5), although on the whole more effectively and permanently by salicylate. In four cases [patients, 6 (J. D.), 9 (L. S.), 8 (J. T.) and 5 (H. G.)] the temperature fell to normal and remained practically unchanged by the nonsalicyl medication. In four cases [3 (M. A.), 4 (T. F.), 5 (H. G.), 7 (S. R.)] the temperature had fallen to normal before the salicylate was administered, therefore the return of the temperature to normal can not be justly attributed as due to salicyl. In two cases [3 (M. A.) in part, and 8 (J. T.) entirely] the febrile temperatures persisted in spite of the administration of salicyl. It appears that once the fever has run its course it tends to abate in spite of the antipyretics used and seldom returns to the original level. Continuous though moderate medication with salicyl or other antipyretics during the period of convalescence, will, of course, tend to mitigate any tendency to a recurrence of the fever. This, as a matter of fact, is a common practice and undoubtedly contributes also to the general recovery of the individual.

Of the eight patients receiving salicylate alone (see Fig. 2), four (11, 12, 5, 21a) continued afebrile though variable temperature. In one (Patient 1) the temperature was reduced to normal and subnormal after repeated salicyl medication only. In the remaining three patients, single administrations of toxic doses of salicyl brought the temperature promptly and permanently within the normal range.

JOINT SYMPTOMS

Pain, tenderness, complaint of "soreness" when movements were attempted, and swelling were the most prominent and constant symptoms in our series before the administration of any medication whatsoever. These were completely relieved, though temporarily in some, in a majority [eight, Patients 1 (E. S.), 2 (J. S.), 3 (M. A.), 5 (H. G.), 6 (J. D.), 7 (S. R.), 8 (J. T.), 9 (L. S.)] of the patients while receiving nonsalicyl medication, and in two patients [6 (J. D.), 9 (L. S.)] no salicyl medication was necessary. The remaining patients [1 (E. S.), 2 (J. S.), 3 (M. A.), 4 (T. F.), 5 (H. G.), 7 (S. R.), 8 (J. T.)] received salicylate because some of the symptoms reappeared in more or less aggravated form after the nonsalicyl medication was stopped. Salicylate removed these symptoms completely in four patients [2 (J. S.), 1 (E. S.), 3 (M. A.), 7 (S. R.)], partially in two [4 (T. F.), 5 (H. G.)]. In two [5 (H. G.), 8 (J. T.)] cases salicyl was ineffective. To what extent the elements of rest and natural recovery contributed in finally obtaining relief during the salicyl régime can not be said, but certainly can not be disregarded. The salicyl periods are not strictly comparable with the nonsalicyl, for salicylate was admin-

istered continuously over a long period, while the nonsalicyl medication lasted only a comparatively short period. This could not be avoided for it was not certain in the beginning of the work if, when results were not satisfactory, during the nonsalicyl régime we were not really depriving the patients of benefits to be derived from salicylate. However, the satisfactory results in patients 6 (J. D.) and 9 (L. S.) obtained without any salicylate whatsoever entirely dissipated our fears, and conclusively demonstrated that complete therapeutic relief can be obtained on a régime of nonsalicyl medication. This completely discounts the claims of specificity of salicylate in rheumatic fever for the joint symptoms and fever at least.

Our records, when salicylate alone was used, are too incomplete to draw any definite conclusions. However, a study of the protocols indicates that salicylate promptly and effectively removed the joint symptoms in a majority of the patients, and this is in harmony with the usual experience. In two individuals (Patients 1 and 21a) it was necessary to repeat the administration of salicylate because the joint symptoms persisted.

GENERAL DISCOMFORT

Under this are included various complaints such as the subjective sensation of aching, weakness and stiffness in the limbs, restlessness, etc. All of the patients became more comfortable on the nonsalicyl combination, only one [4 (T. F.)] having complained of some discomfort. Two [6 (J. D.), 9 (L. S.)] became entirely comfortable without further (salicyl) medication.

With six of the patients receiving nonsalicyl medication discomfort returned and they became comfortable, though partially with one [2 (J. S.)], again on salicyl medication. Discomfort with one [8 (J. T.)] continued in spite of repeated administration of salicylate, general comfort being restored with nonsalicyl medication.

Our notes on the series in which salicyl alone was administered are incomplete.

CIRCULATION AND RESPIRATION

The tabulated results show that both the pulse and respiration were usually showed with the defervescence of the fever irrespective of the kind of medication, i. e., whether nonsalicyl combinations or salicylate, although there appeared to be a greater tendency to slowing of the respiration with the opiates. The differences were unimportant, and since these functions have no important bearing on the symptomatic relief in rheumatism, they need not be considered further.

It is well known that endocarditis, which is commonly associated with rheumatism, is not remedied by the administration of salicylate. This was true for our salicylate series, and the same also held for the nonsalicyl.

DURATION OF DISEASE

This will vary with the initial severity of the attack, multiple extension to joints, the individual, and other factors. Our series are too small to furnish

definite conclusions. However, a comparison of the nonsalicyl-salicyl with the salicyl alone series may be made. In the nonsalicyl-salicyl series seven patients [1 (E. E.), 2 (J. S.), 3 (M. A.), 4 (T. F.), 5 (H. G.), 7 (S. R.), 8 (J. T.)] the sojourn in the hospital ranged from 17 to 31 days, mean 24 days. Two patients [6 (J. D.), 9(L. S.)] receiving nonsalicyl medication alone sojourned only 8 and 19 days, respectively. With eight patients of the salicyl series the sojourn ranged from 6 to 38 days, mean 15 days. In general this would be favorable to salicylate. However, there were great variations, and a larger series would likely smooth out the differences. Assuming these results express the general tendency correctly it seems hardly possible that special claims to specificity of salicylate in rheumatism could safely rest on this criterion, for the sojourn is about as short on nonsalicyl medication alone as on salicylate alone, and the tendency to prolongation in the nonsalicyl-salicyl series, taking the cases individually is practically unimportant.

RECURRENCE OF SYMPTOMS

In 7 out of 9 patients whose initial medication consisted of various nonsalicyl combinations, symptoms of the disease recurred. Of these one [8 (J. T.)], however, was not benefited by salicyl treatment; and two patients had no recurrence after nonsalicyl medication. Of the salicyl series, consisting of 8 individuals, two required repeated salicyl treatment for a recurrence of the symptoms. It would seem, therefore, that treatment with salicylate alone from the beginning insures freedom from symptoms of the disease for a majority of patients, and this agrees with the usual experience; but it is also true that treatment with nonsalicyl combinations alone can render patients [see 6 (J. D.) and 9 (L. S.)] free of the symptoms. This does not point to any particular specificity of salicylate. The greater efficiency of the salicyl may be ascribed to the massive doses and prolonged treatment.

A summary of all the results as to dosage and therapeutic response in all the patients is presented in Table I.

DISCUSSION

From this study of the comparative effects of nonsalicyl and salicyl medication, it can not be concluded that salicylate possesses any unusual action or peculiar specificity in rheumatic fever. It is seen that prompt though partial relief was obtained in the majority of the patients receiving drugs other than salicyl. This is true for both early and late symptoms of the disease. In some of the patients the symptoms persisted despite salicyl medication, and in at least 4 cases (2 of nonsalicyl-salicyl series and 2 of salicyl) the condition recurred shortly after salicyl treatment. In those patients in whom the symptoms persisted, although considerably moderated, after treatment with nonsalicyl antipyretics and analgesics, salicyl appeared to give more permanent relief. On the other hand in two of the patients the fever persisted in spite of the salicyl medication. In some of the patients the persisting antipyretic effect during salicyl medication (although other symptoms of the disease were present) may be due to the retention or delayed action of the nonsalicyl antipyretic.

TABLE I

COMPARATIVE THERAPEUTIC RESPONSES OF RHEUMATIC INDIVIDUALS TO NONSALICYL AND SALICYLATE MEDICATIONS

PATIENT	NATURE OF THERAPY				
	NONSALICYL			SALICYLATE	
	DRUGS AND TOTAL DOSAGE		RELIEF	TOTAL DOSAGE	RELIEF
1 (E. S.)	Quinine 190 gr.	Morphine 1½ gr.	Partial	Sod. Salicylate 1600 gr.	Complete
2 (J. S.)	Quinine 270 gr.	Morphine 4 gr.	Partial	Sod. Salicylate 460 gr. $NaHCO_3$ 460 gr.	Partial
3 (M. A.)	Quinine 170 gr.	Morphine 2¼ gr.	Partial	Sod. Salicylate 1063 gr.	Partial
4 (J. F.)	Quinine 190 gr. Phenacetine 160 gr.	Morphine 9 gr.	Partial	Sod. Salicylate 1620 gr.	Partial
5 (H. G.)	Phenacetine 230 gr.	Morphine 5¾ gr.	Partial	Sod. Salicylate 220 gr.	Partial though more complete
6 (J. D.)	Phenacetine 30 gr.	Morphine ¾ gr.	Complete	None administered	
7 (S. R.)	Phenacetine 160 gr.	Morphine 4 gr.	Partial	Sod. Salicylate 140 gr.	More complete
8 (J. T.)	Phenacetine 130 gr. Antipyrin 50 gr.	Morphine 3½ gr. Papaverine 3 gr.	Temporarily complete Complete	Sod. Salicylate 840 gr.	None
9 (L. S.)	Quinine 20 gr.	Papaverine 2 gr.	Complete	None administered	

With four of the nine patients [1 (E. S.), 3 (M. A.), 4 (T. F.), 7 (S. R.)] unquestionably no effective and permanent relief from the symptoms of pain, fever, swelling of the joints, and general discomfort, was obtained until salicylate was administered. Eliminating the elements of time, rest, and natural recovery, it appears that the relief of later symptoms is brought about more effectively and permanently by salicyl than by combinations of drugs whose pharmacologic actions are similar, but different chemically.

The results of a previous statistical study[3] support the provisional conclusions drawn from the present work. It was found that about 18 per cent of the patients with rheumatic fever were incompletely or not at all relieved by the administration of salicylate in toxic doses. In the large majority that was relieved it is not known to what extent repeated salicyl medication was resorted to, but it is certain that salicyl was repeatedly administered to many patients. In addition, complete relief was obtained in a majority of individuals suffering with other diseased conditions, and whose etiology was either questionable or entirely different from rheumatic fever. That is, 53 per cent of cases of chronic rheumatism and 41.6 per cent of a miscellaneous variety of other conditions were completely relieved of their symptoms by the administration of salicylate in toxic doses. This favorable influence exerted by salicylate would

not, of course, deprive salicylate of its alleged specificity in rheumatic fever but the symptomatic relief (analgesia and antipyresis) produced by it is in line with that obtained in the treatment of rheumatic fever. It is conceivable at least that this is also the main contribution of salicylate in the generally practiced therapy of rheumatic fever.

CONCLUSIONS

The number of our cases is too small to draw definite conclusions. However, this much may be said, namely, that so far as the acute symptoms of rheumatic fever are concerned, these can be promptly and effectively relieved by combinations of antipyretics and analgesics chemically different from salicylate. It is also possible to obtain permanent relief with these. If to this are added the favorable reports of J. L. Miller with foreign protein and rest alone, and the numerous recurrences of the disease in patients repeatedly treated with salicylate in large doses, then it may be provisionally concluded that salicylate possesses no thoroughly demonstrated specific action in rheumatic fever. It is no more than a symptomatic remedy which can be safely administered in very large doses, and represents a fortunate combination of both antipyretic and analgesic qualities which makes it much more suitable, and, also desirable for the treatment of rheumatic fever than combinations of opiates and various antipyretics. The injurious effects of salicylate on renal function and the kidney[4] might be raised against the promiscuous and unwarranted use of the drug, but its efficiency and desirability as a symptomatic remedy in rheumatic fever may be regarded as outweighing the seriousness of these disturbances.

SUMMARIZED PROTOCOLS

Patient 1 (*E. S.*). *Female. Diagnosis*—rheumatic fever. Temperature on admission 100.4° F. Administered 180 grains of quinine together with 1½ grains of morphine during the first 5 days of illness. During this time the temperature was variable though generally slightly elevated with an improvement in general discomfort and freedom from pain and tenderness in the joints. On the sixth day there was general discomfort but no pain in the joints, the temperature remaining elevated. Salicylate to "toxicity" (180 grains) was administered, and was continued every four hours for the next 13 days, when the patient was discharged cured. During the salicyl period the patient was generally comfortable and free from joint pains and fever. The temperature gradually fell to the normal level and towards the end became subnormal. The total dosage of salicyl administered was 1600 grains.

It may be concluded that nonsalicyl medication, consisting of morphine and quinine, partially removed the symptoms of rheumatic fever the temperature remaining practically unchanged. This, together with the remaining symptoms were completely removed by prolonged treatment with salicyl.

Patient 2 (*J. S.*). *Diagnosis*—rheumatic fever. Temperature on admission 102.3° F. Administered 270 grains of quinine together with 4 grains of morphine during the first five days. The temperature gradually fell to 97.8° on the third day, and again gradually rose, reaching 102° at the end of the fifth day. During the time the temperature fell the patient was free from pains in the joints and was generally comfortable, but as the temperature rose symptoms of general discomfort together with marked pain in the joints originally affected returned. On the sixth day the patient was made toxic with 240 grains of salicylate, and the drug was continued every four hours for the next few days equivalent to about 220 grains, or a total of 460 grains of salicyl was administered. Pain in the joints and general discomfort promptly disappeared and the temperature fell to 97° F., and remained practically normal for the next four days, but on the twelfth day the temperature rose to 100°, and after that gradually fell to 99°, that is, the patient was

febrile to the end of the experiment. During this time there was general discomfort and the wrists and shoulders were painful until the 16th day. During the last two days the patient was comfortable without complaint of pain and was discharged on the 18th day.

Both the nonsalicyl and salicyl medications gave partial relief from symptoms of rheumatic fever, the symptoms of the disease returning rather promptly after discontinuance of both types of medication. From this salicyl would not appear to be any more specific and curative than quinine and morphine.

Patient 3 (*M. A.*). *Diagnosis*—rheumatic fever. Temperature on admission, 102.3° F. Administered 2¼ grains morphine together with 170 grains of quinine during the first five days, with partial improvement of the condition. The joint pains disappeared so that the patient could easily roll in bed. The temperature fell to normal on the third day and gradually rose, remaining at a level between 99 and 101° for the next two days. On the sixth day of the disease 17.1 gm. (263 grains) of salicyl was administered to "toxicity" owing to the return of pain and swelling in the joints originally involved, fever and general discomfort. The temperature fell promptly to normal on the following day and the patient was free from pain and generally comfortable. This lasted only during the next day. On the eighth day fever, pains, and tenderness in the joints, and general discomfort reappeared and remained unchanged, except for the temperature which showed a tendency to return to the normal, until the patient was made "toxic" again on the tenth day with 200 grains of salicyl. After this, and for the next six days, the temperature tended to remain above normal (moderate fever), but the symptoms of pain and general discomfort disappeared. On the seventeenth day salicyl medication 10 grains every two hours was begun, and maintained until the twenty-first day, or the end of the patient's sojourn in the hospital. His condition remained unchanged, that is, there seemed to be complete relief brought about by the salicyl, a total of 70 gm. (1078 grains) having been administered.

About a month later the patient returned to the hospital with another attack of rheumatic fever which was successfully treated by means of salicyl and prolonged rest in bed.

It may be concluded that partial relief was obtained by the administration of morphine and quinine and salicylate and that this was more complete after the repeated administration of a large quantity of salicyl. However, the condition recurred in its original severity. Therefore, it appears doubtful if salicyl possesses a specific curative property in rheumatism.

Patient 4 (*T. F.*). *Diagnosis*—rheumatic fever. Temperature on admission 101° F. Administered ¼ grain morphine hypodermically, together with 10 grains of phenacetine by mouth every 2 hours for 2½ days, then morphine and quinine in the same dosage for one day. A total dosage of quinine sulphate 130 grains, morphine sulphate 7½ grains, and phenacetine 160 grains, both administered during the first four and one-half days of the disease. During this time there was a temporary (for 2 days) relief from fever and then the temperature gradually rose; some amelioration of discomfort and disappearance of pain in some joints on the second day of treatment, but the pain gradually increased and progressively involved other joints together with increased discomfort. Patient was now made toxic with 20.8 gm. (330 grains) of salicylate. For the next 2 days the temperature fell, ranging from subnormal to normal, and the patient was free from pain and was comfortable. After this the temperature gradually rose and symptoms of pain and discomfort increased. Morphine 1½ grains, together with quinine 60 grains were administered during the next two days without amelioration of pain in the joints and general discomfort; and the temperature remained about normal with small oscillations above and below the normal for 3 days. With the exception of the temperature which tended to remain subnormal, the symptoms persisted in more or less aggravated form for the next 42 days, or until the end of the 51st day of the disease, being relieved only when the patient was made toxic by salicylate, and during this time 8 toxic doses and intermediary salicyl medication, or a total of 1300 grains were administered. The patient received a grand total of 1620 grains of salicylate.

It may be concluded that partial relief was obtained with both nonsalicyl and salicyl medications but the relief appeared to be somewhat more complete with repeated salicyl treatment although it was difficult to discount the psychic element.

Patient 5 (*H. G.*). *Diagnosis*—rheumatic fever. Temperature on admission 104° F. During the first three days of disease 4½ grains of morphine and 180 grains of phenacetine were administered, and on four different days during the next eight days one grain of

morphine and 40 grains of phenacetine were administered, making a total of 5½ grains of morphine and 220 grains of phenacetine during the first eleven days of illness. The temperature returned to normal on the second day of disease, rose to 101.4° on the third, and fell to normal on the fourth day, remaining subnormal from the sixth to the fourteenth days. The original severity of the joint symptoms such as pain, swelling and redness gradually disappeared and on the seventh day the patient felt well enough to get up, but the symptoms gradually reappeared together with a marked rise in temperature on the fourteenth day the pain reappearing in the same (knee) joint, and further medication was necessary. The patient was made "toxic" with 140 grains of salicyl, the temperature fell, and the patient was comfortable during the next two days. However, on the seventeenth day the pain in the joints reappeared together with a slight elevation in temperature. Morphine, ¼ grain, and phenacetine, 10 grains, were administered. The pain in the knees was temporarily relieved. Salicyl to "toxicity" (180 grains) was administered on the twenty-second day, with recovery of pain in the left knee joint, the right knee remaining stiff and painful to the end of the patient's sojourn in the hospital, i. e., the twenty-seventh day.

Prompt though partial and temporary recovery followed nonsalicyl medication in the beginning of the disease. The administration of salicyl gave further relief but no complete recovery.

Patient 6 (*J. D.*). *Diagnosis*– rheumatic fever (relatively mild attack). Temperature on admission, 101.4° F. Administered phenacetine 10 grains together with morphine ¼ grain each day during the first two and on the fourth days; administered a total of phenacetine 30 grains, morphine ¾ grain. During this time, the patient was fairly comfortable although pain in the joints persisted and remained unchanged. The temperature fell to normal after the second dose of the drugs and then returned to 100°, and again fell to 97° on the fourth day, returning to 99.8° on the fifth day. After the fifth day, and to the end of the patient's sojourn in the hospital (end of fourteenth day), the temperature remained subnormal, and all symptoms of the disease disappeared completely, without further medication of any kind. The disappearance of all the symptoms coincided with the fall of temperature on the fifth day, the patient making an uneventful recovery in the next ten days.

In this patient, therefore, complete relief was obtained without salicyl medication.

Patient 7 (*S. R.*). *Diagnosis*—Rheumatic fever. Temperature on admission was 100° F. On the first day 50 grains of phenacetine and 1¼ grains of morphine were administered, with fall of temperature to 97° and complete relief from symptoms of pain in joints and general discomfort for 3 days. On the fourth day, the temperature rose to 100°, and pain in the same joints (left elbow and shoulder) returned. This continued in more or less aggravated form, despite the administration of single daily doses of phenacetine (10 grains) together with morphine (¼ grain) for the next eight days. During this time there were daily changes in temperature ranging from normal in the morning to a moderate fever of 100° in the afternoon. There was no general marked discomfort complained of. A total dosage of 160 grains of phenacetine and 4 grains of morphine had been administered. However, on the eleventh day the patient received a toxic dose of salicylate amounting to 140 grains. The temperature had returned to normal the day before the administration of salicyl and tended to remain subnormal for the next six days. Pain in the joints disappeared and the general condition of the patient improved. On the fifteenth day the patient was discharged completely relieved of symptoms of rheumatic fever.

The symptoms of rheumatic fever were partially though temporarily relieved by the administration of phenacetine and morphine in the beginning of illness, and although the temperature returned to normal before the administration of salicyl was begun, it is seen that more complete relief from the remaining symptoms ensued after salicyl.

Patient 8 (*J. T.*). *Diagnosis*—rheumatic fever. Temperature on admission 100.4° F. Administered 3½ grains of morphine together with 130 grains of phenacetine during the first three days of illness. There was a fall of temperature to 98° on the second day, and remained subnormal with small variations for the next seven days. After the third day the patient remained free from pain and other symptoms for the next seven days. Symptoms of pain, redness, and swelling in joints, general discomfort and fever, returned on the tenth day. The patient was made "toxic" with 300 grains of salicylate, and during the next three days 540 grains of salicyl were administered, or a total of 840 grains without relief of pain and other symptoms in the joints, the temperature, however, remaining

subnormal. In fact, the patient's condition was worse than on admission. The patient now (on the fifteenth day) received 10 grains of antipyrine and remained in bed for the next two days, with the relief of symptoms in some of the joints, but other joints continued to be involved. During the next three days 3 grains of papaverine together with 30 grains of antipyrine were administered. The temperature remained subnormal during the remaining sojourn in the hospital, or the end of the 36th day, and the symptoms of pain and swelling in joints, and general discomfort gradually disappeared, although some stiffness in the joints persisted.

Nonsalicyl medication gave prompt and practically complete relief from the symptoms of rheumatism during the first attack. Salicylate in large doses was ineffective during the second attack, but complete relief ensued following the administration of antipyrine and papaverine. This does not speak favorably for salicylate.

Patient 9 (*L. S.*). *Diagnosis*—rheumatic fever. Temperature on admission 104.6° F. For two days previously had received unknown quantity of salicyl, became "toxic," but without relief of joint symptoms and fever. Patient was brought into hospital on last day of salicyl treatment, his condition being more aggravated. That night patient received 2 grains of papaverine together with 20 grains of quinine. On the following day, the temperature fell to 97°, rose to 100° on the second day, and again to 100.8° on the third day, and then gradually fell to normal on the fifth day, and remained unchanged till the end of the eighth day, when he was discharged. Following the administration of papaverine and quinine the patient was more comfortable and the symptoms of swelling, pain, and redness in the joints gradually disappeared, so that by the end of the fourth day the patient had obtained complete relief from all symptoms of the disease, and remained so until the date of his discharge.

No relief in this patient was obtained by salicyl medication; complete relief followed the administration of two doses of papaverine and quinine. It is possible that the patient would have recovered without any medication after the salicyl period.

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CLINICAL MANIFESTATIONS OF EMPYEMA*

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WERE the physical signs in all cases of empyema the same, the problem of recognition and of proper treatment would be comparatively simple. But just as the proper indications for operation may vary with each case, so in no two cases may the evidence of pleural pus be said to be identical. Nevertheless, for convenience, and in an attempt to clarify the problem, we have classified the various empyema cases as seen on the medical service into certain groups, the individual members of which present in a general way the same history, course and physical findings. The following nomenclature has been chosen as being descriptive of either the clinical or the anatomical manifestations in the different groups:

I. Primary empyema.
II. Precocious empyema.
III. Cryptic empyema.
IV. Massive empyema.
V. Suppurative polyserositis.
VI. Interlobar empyema.
VII. Juxtamediastinal pus.
VIII. Polylocular empyema.
IX. Latent empyema.

I. PRIMARY EMPYEMA

This group comprises a few patients who have been admitted suffering from an illness of but short duration, the onset of which has been sudden with chills, fever, and pleural pain, and on whom the diagnosis of lobar pneumonia has usually been previously made. The physical findings on admission may be those of a large fluid accumulation, dullness to flatness with absent tactile fremitus, and diminished or absent breath and voice sounds, or the voice sounds may be fairly well transmitted. Fluid is at once suspected and thoracentesis confirms the diagnosis. In some of these cases it is difficult to state whether the empyema is primary or whether it is secondary to an intrapulmonary condition. We have found the character of the sputum to be of material aid in thus distinguishing a primary empyema. In it there is neither the tenacious sputum of lobar consolidation nor is there the easily raised muco-pus of bronchopneumonia. Cough may be present and urgent but it is quite nonproductive.

We have had two cases of primary empyema in our operated series, one of whom gave a history of recent measles infection while the other did not. Of how great importance the measles could be in predisposing to involvement of

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the pleural cavity can be but a matter of conjecture. In this camp the pneumococcus has been the organism found in the pleural exudate.

In addition we have had two cases of primary serofibrinous pleurisy in whom the chest fluid contained pneumococci. Both patients were aspirated repeatedly and the first recovered without operation while the second finally developed frank pus and was drained surgically.

II. PRECOCIOUS EMPYEMA

It is a common saying that if the temperature in a case of lobar pneumonia remains up after the seventh to the tenth day of the disease it is well to suspect a complicating empyema. It is indeed true in our experience that following frank lobar penumonia true pus did not appear in the pleural cavity in the majority of cases until after the time for crisis. Of twenty-five cases in which the date of empyema diagnosis is definite, only one had the complication previous to the seventh day, and that on the second day. Four cases occurred on the tenth day, three on the twelfth and one or two occurred on other days from the seventh as late as the thirty-seventh.

But it would be negligence to wait until the seventh day before beginning the search for empyema. The majority of the cases develop, first, a serofibrinous pleurisy containing organisms and, later, pus. Although the latter has occurred in lobar pneumonia after the seventh day, the former in two-thirds of the cases was proved by thoracentesis to be present previous to the seventh day. Upon the early recognition and repeated aspiration of this clear fluid frequently depends the possibility of avoiding subsequent rib resection.

Amongst the postinfluenzal group of pneumonias which occurred during the spring frank pus developed more rapidly than in the primary lobar pneumonias. Of seven such cases five developed pus previous to the sixth day.

To summarize, we have had four cases of precocious empyema following lobar pneumonia, one on the first day, two on the second and one on the third. Two more are noted among the postinfluenzal cases as occurring on the fifth day. In all other cases in which the information is exact, pus did not occur until after the seventh day. Among the bronchopneumonias also precocious empyema is the exception. The majority of cases were discovered after the ninth day.

III. CRYPTIC EMPYEMA

One feature of the empyema problem that has elicited comment from several camps is the apparent fact that our previous teachings concerning the physical indications of pleural fluid are erroneous as regards the postbronchopneumonia empyemata. It is true that most of the cases occurring during the severe bronchopneumonia epidemic did not show typical signs of fluid. But as we have become better acquainted with this type of chest we have concluded, not that the old signs of fluid are at fault, but that their enumeration must be modified by certain exceptions and amplifications. It is difficult and in occasional instances nearly impossible to demonstrate fluid from the physical findings in the bronchopneumonias that we have had in camp, but that it can be done is indicated by the fact that, since the latter part of December, 1917, scarcely a

case with pleural fluid has gone to autopsy undiagnosed, even though the amount be small.

Perhaps the most disturbing finding over fluid is the presence of rales. Coarse, moist, sticky rales may be heard over a fluid which nearly half fills one side of the chest. It is never safe to decide, because rales are present and seem close to the ear, that fluid is absent. We do not recall, however, having heard the typical fine crepitations of pneumonic consolidation over fluid.

Among the signs indicative of fluid in bronchopneumonia there are two of paramount importance. First of these should be mentioned diminished or absent breath sounds. Where breath sounds are distant and even though dullness be but moderate and rales be present, fluid should be suspected. Flatness to percussion, best determined by comparison with percussion over the deltoid muscle, is a frequent indication of fluid in bronchopneumonia. Also in cases showing dullness without true flatness and with distant breath sounds, fluid is to be suspected.

The presence or absence of a Grocco's paravertebral triangle or of transmitted tactile fremitus have been only of confirmatory value. Displacement of the heart borders, the apex impulse or the point of maximum intensity of the heart sounds is frequently a valuable diagnostic aid. The patient's general condition is of aid in lobar pneumonia but in bronchopneumonia, the sweating, cyanosis and wide diurnal temperature excursions are nearly as frequent where empyema is absent as when it is present.

In choosing the point for thoracentesis one is governed, at times, by the flatness of the percussion note and, at times, by the diminution of the breathing and of the whispered voice. It frequently is necessary to insert the needle to a considerable distance before fluid is reached. Another surprising observation is the relatively large amount of fluid that may be obtained at operation, even though two or three previous needlings, within a rather limited area, were necessary before it could be found. Provided there is strong evidence that fluid is present, one should not rest content with a single nonproductive needling. Thoracentesis should be persisted in until there is no longer any uncertainty. Usually two, or at the most three, needlings will definitely settle the question.

The frequent accumulation of encapsulated fluid in bronchopneumonia would appear to be the explanation for the anomalous signs in empyema. Congestion and compression of the surrounding pulmonary tissues accounts in part, at least, for the presence of rales. In lobar pneumonia, cryptic empyema is less frequently present and the classical signs of fluid are in evidence.

IV. MASSIVE EMPYEMA

This well-known condition has occurred in a small number of our series. More frequently the pyothorax is walled off by adhesions and limited in its extent. In the larger effusions and in those loculated effusions which occur in the region of the left axilla, displacement of the heart and Grocco's sign have been of assistance. Information obtained from examination for tactile fremitus has varied directly with the size of the fluid accumulation, fremitus being characteristically absent over the massive empyemata.

V. SUPPURATIVE POLYSEROSITIS

This condition deserves mention chiefly because of its comparative infrequency. We have chosen this name to designate those cases following lobar, or more particularly bronchopneumonia, in which at autopsy there is found to be present a bilateral empyema, a purulent pericarditis, and a general peritonitis. In our series we have had but two cases showing all of these findings but have had three or four additional in whom peritonitis occurred as a complication to pneumonia, and in one of these there was also a unilateral empyema. In the case of two patients who were first operated for appendicitis, subsequently developed pneumonia and finally terminated with peritonitis, the pneumococcus was found to be the organism invading the peritoneum. We have had two cases with bilateral empyema and suppurative pericarditis as instances of a form of suppurative polyserositis.

The problem as to whether spread to other serous cavities is metastatic or by direct invasion through the diaphragm or pericardium is unsettled. There are those who claim that pericarditis complicating pneumonia results from direct spread, but the occurrence of pericarditis or peritonitis in pneumonia cases without empyema seems scarcely explainable by such an hypothesis.

Pneumococcus peritonitis, as it has occurred in this camp, is evidenced by few symptoms. There may be some distention and but moderate rigidity and tenderness. Or the symptoms may be very definite. At autopsy one finds small collections of sweet-smelling, greenish-yellow pus lying between the folds of the intestines and settled in the dependent fossae. The distribution is usually throughout the entire peritoneum.

VI. INTERLOBAR EMPYEMA

This has been observed in a few instances at autopsy. Among those who have survived, its possible presence is frequently indicated first, by the x-ray, second, by the fact that signs of fluid are not definite, and third, by the fact that it frequently is necessary to insert the needle to a considerable depth before fluid may be obtained. We have had three typical cases of right interlobar empyema in which fluid could be obtained only from the region covered by the midscapula when in its normal position and then, only after the needle had been inserted to its full extent. In these cases the most useful physical sign was flatness to percussion after the scapula had been moved well out of the way. The x-ray gives valuable assistance in these cases.

VII. JUXTAMEDIASTINAL PUS

So frequent have been our cases of loculated empyema between the visceral pleura and pericardium or upper mediastinum, that we have included them in our classification as a distinct group. Particularly has this condition been found to be present at autopsy. Among the earlier cases of our series there was one patient who had developed a postpneumonia empyema and who had been drained surgically. He had been doing fairly well and the drainage had become quite scant when, unexpectedly, his condition became worse, and

in spite of attempts to locate more pus he died. At autopsy the drainage was found to be quite complete in the cavity drained but between the lung and the upper mediastinum there was a considerable walled-off accumulation of pure pus. We have also been able to find this condition during life and, through appropriate treatment, to cure the patient. Here, again, the x-ray is of inestimable value.

Instances have been found at autopsy of suppurative mediastinitis. We have one patient at present on the ward who shows the classical signs of this condition, substernal pain, increase in mediastinal dullness and in mediastinal shadow by x-ray, unequal pupils and pulses, and the constitutional signs of pus. More recent x-rays show evidence of encapsulation adjacent to the upper mediastinum and it is possible that this case is not one of suppurative mediastinitis but juxta-mediastinal empyema. He is progressing favorably.

VIII. POLYLOCULAR EMPYEMA

A condition of considerable importance is the presence in the same chest of more than one loculated fluid collection. We have had two patients in whom we were able to obtain clear serous fluid from one area and pus from another. The case cited under juxtamediastinal pus is another example. One fluid collection may be parietal while the second is interlobar and under these circumstances the latter is especially liable to be missed. Associated with the condition of polylocular empyema should be mentioned an occasional finding in drainage cases where the temperature remains elevated although the discharge has become scanty. This is frequently due to walled-off pus which the tube no longer reaches. In all of the above conditions the x-ray gives considerable aid.

IX. LATENT EMPYEMA

In decided contrast to those individuals in bronchopneumonia whose condition rapidly becomes critical, with accumulation of serofibrino-purulent fluid in the pleural cavity and who die even before the fluid has opportunity to become real pus, are occasional cases who may carry about, without reaction, a chest nearly full of pus. One patient in our earlier series carried about with him an empyema which had escaped detection until the physical examination preliminary to discharge. Pus was found on the thirty-seventh day after his pneumonia and after his temperature had remained normal for fourteen days. After removal of the pus, the patient was discharged well.

USEFULNESS OF THE X-RAY

The x-ray has two fields of usefulness which easily render its aid indispensable. The first of these is the possibility of thus discovering interlobar empyema, juxtamediastinal pus and polylocular fluid. The second and equally important phase of the x-ray work is in the examination of convalescent empyema patients who have been up and about for some time, who do not regain strength as they should do and who occasionally have a mild temperature elevation. In these, radiograms at times demonstrate a small pocket of sacculated

pus sometimes contained together with air in a thick walled cavity. Aspiration without operation, provided the fluid is small in amount, sometimes produces satisfactory results.

MEDICAL "FOLLOW-UP" TREATMENT

We would emphasize the importance of medical "follow-up" work on post-operative cases. It has been the custom in this hospital for the man who has general supervision of the pneumonia cases to devote a portion of his time to examination of empyema cases on the surgical wards. He makes daily examinations of acutely ill patients and notes his findings on the clinical record, together with whatever recommendations he considers advisable. Search is made for evidences of retained pus and for complications, particularly pericarditis, peritonitis and beginning fluid accumulation on the well side of the chest. In a few patients signs of considerable fluid remained even though the drainage tube appeared to be functioning properly. Following the recommendations of the medical man adhesions were broken up and the walled-off pus was evacuated. The presence of a drainage tube is no counterindication to the use of the exploratory needle in cases where there is a question as to the persistence of pus.

COCAINE POISONING. REPORT OF A CASE WITH NECROPSY*

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SINCE the advent of local anesthesia, practically all who have had extensive experience with the various preparations have at times encountered instances of acute poisoning and occasionally death immediately after their use. Fatal cases are not exceedingly rare and it is certain that many deaths due to the anesthetic are not so recorded. Cocaine hydrochloride as used clinically appears to be particularly toxic, since symptoms of poisoning occur quite frequently even after the use of small quantities. There are, however, considering the widespread use of cocaine, but comparatively few fatal cases reported. Witthaus and Becker state that up to 1911 only sixty-seven deaths from cocaine have been reported and from 1911 to date only seven reports of fatal cases have been added. In a rather extensive pathologic experience the case herein recorded is the first instance in which a necropsy has been secured by us. Because of the rarity of such examinations and furthermore since the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association have particularly requested all available data, this accidental death following the use of cocaine is described although the clinical history is rather brief.

Clinical History.—The patient, a man, forty-six years of age, an agent, complained of pain in the lower right quadrant of the abdomen. On the preceding day he suffered from "colic" and vomited three times. Temperature 100° F., pulse 96, respirations 24. Patient entered the hospital and the appendix was removed.

That night at 12 P.M. the resident physician attempted twice to catheterize the patient but without success. Slight bleeding followed each attempt. About two hours later, "three drams of a 4 per cent cocaine solution were injected into the urethra. The patient immediately had a convulsion and died."

Necropsy.—Twelve hours postmortem. Body length 180 cm.

The body is that of a well-built, well-developed white male adult. Rigor mortis is present. There is very slight postmortem lividity in the dependent portions. There is no edema of the extremities and no general glandular enlargement. The pupils are midwide and equal. To the right of the umbilicus is a recent appendectomy wound.

Peritoneal Cavity.—The surfaces are normally smooth, moist and glistening. The stomach is slightly dilated. The appendix has been removed and the site of operation appears clean, but blood stained. A small quantity of fluid blood is found in the right iliac fossa. The adjacent coils of intestine are slightly injected and adherent.

Pleural Cavities.—The surfaces appear negative. A few adhesions are found about the upper lobes on each side. An occasional area of brownish pigmentation is also present.

Lungs.—The right lung is somewhat voluminous and the left is collapsed. Both show moderate congestion but crepitation is present except in the lower lobes which are dark red on section and filled with fluid blood. Dissection of the large vessels shows no thrombi or emboli.

Heart.—It weighs 320 grams. All cavities appear to be dilated, particularly the right side, where a large quantity of fluid blood is found. The blood is dark red in color and only a few small clots are present. The pericardium is negative. The endocardium and valves also appear normal. The coronary arteries are patent throughout and no narrowing of the lumen is found. The myocardium is dull red and unusually soft and flabby. The ventricular walls are thinner than normal, the left being 1.5 cm.

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in thickness. Nothing unusual is found on section. The pulmonary artery is opened in situ and no thrombi or clots of any description are found.

Gastrointestinal Tract.—The stomach is slightly dilated, but not otherwise abnormal. The mucosa appears negative. The small and large intestines also appear normal. There is no enlargement of the mesenteric lymph nodes.

Pancreas.—It is not remarkable.

Spleen.—Weight 175 grams. It is dull red in color and appears normal.

Liver.—Weight 1850 grams. It is dark red in color. The surface is friable and the hepatic lobules are very distinct. The gall-bladder and bile passages are normal.

Kidneys.—Combined weight 250 grams. They appear small and are dark red in color. The capsule strips readily, leaving a smooth surface. Cut surface is distinctly injected and fluid blood escapes. The pelves and ureters are negative. The bladder is greatly distended, containing approximately one liter of bloody urine in which a few small clots of blood are found.

Genitalia.—The prostate is not enlarged. The prostatic urethra appears normal. On opening the entire length of the urethra, the surface appears smooth and normal. No areas of ulceration are found. The lacunæ are prominent. The testicles are normal.

Aorta.—It is normal throughout.

Brain.—Weight 1400 grams. The dura and inner surface of the calvarium are normal. The pia-arachnoid is distinctly edematous and injected. Serial sections are made and nothing pathologic found.

ANATOMICAL DIAGNOSES.—Acute dilatation of heart, acute congestion of liver, kidneys, spleen and lungs; edema of cerebral meninges, chronic pleuritis, absence of appendix (operation).

MICROSCOPIC EXAMINATION.—

Heart.—There is marked "fragmentation" of the muscle fibers. The capillaries are not unusually distended, but an occasional area of interstitial hemorrhage is found. Pigment is not increased and the nuclei appear normal. Sections show the right ventricular wall to be unusually thin, otherwise negative. There is no increased amount of fat present.

Liver.—There are no marked alterations. The sinusoids adjacent to Glisson's capsule are distended with blood. Elsewhere they are somewhat less congested.

Spleen.—Great engorgement, with interstitial hemorrhage. The smaller vessels show hyalin changes in the intima.

Pancreas.—Not remarkable.

Kidney.—The vessels are greatly distended with blood. Moderate degenerative changes of the tubular epithelium present. The glomeruli are congested. All the tubules adjacent to the capsule are dilated and contain a fibrinous deposit. Similar deposits are found in the glomeruli in this region.

Bladder.—Congestion and edema. Separation of the muscle bundles between which are found a fibrinous deposit and occasional extravasation of blood.

Intestine.—The ileum contains an excessive amount of mucus. Numerous polynuclear leucocytes are found beneath the serosa, in the mesenteric fat and between the muscle bundles.

Cerebrum.—Edema of the cortex. Meninges show marked distention of the vessels, slight cellular infiltration and areas of great pial thickening. The molecular zone presents a rarefied or vacuolated appearance and the nerve cells found within this zone stain poorly as though due to acute degenerative changes.

Cerebellum.—The vessels of the meninges are congested. Slight periadventitial lymphocytosis.

Prostate.—A few areas of lymphocytic infiltration present.

Seminal Vesicles.—Muscular hypertrophy. Very few spermatozoa present. Many of the epithelial cells contain a brownish pigment.

Urine.—Numerous leucocytes, erythrocytes, tailed epithelial cells, spermatozoa and oil droplets are present.

Chemical examination of the urine from the bladder by Doctor Arthur Knudson is negative for cocaine.

The symptoms and death occurring so quickly late at night did not make possible clinical observations other than these already noted. On subsequent inquiry, it was learned that the cocaine used was in the form of a 4 per cent

stock solution and comparatively fresh. The resident physician stated that about three drams were used and this would correspond approximately to 0.50 gram of cocaine hydrochloride. The lethal dose is variably estimated, but generally considered to be less than 1.000 gm. In nearly all urethral cases reported, less than 1 gram has caused death and it is very likely that a much smaller quantity produced the actual poisoning.

Since the publication of Witthaus and Becker but few cases have been recorded, although a number of instances are related where symptoms of poisoning ensued. There is little doubt that many deaths have occurred either accidentally or in the case of cocaine habitues from over dosage. In the cases reported by Witthaus and Becker the dose is stated in but twenty-five and of seven cases recorded since 1911 we find the quantity stated in four. In addition to the fatal cases following the injection of cocaine, many others are reported where the simple application of a 4 per cent solution to burns or ulcers or in the form of a spray in the nose caused death.

The onset of symptoms may be immediate or delayed for several hours. Death usually occurs promptly, but is less likely to happen with an increasing interval of time and rarely takes place after three hours. Excitement and convulsions followed by collapse are the chief symptoms and death appears to be due to cessation of respiration or of heart action.

Nothing characteristic is found at postmortem examination. In our case, dilatation of the heart, acute congestion of the organs and edema of the meninges were the chief changes noted and correspond to the results obtained in previous necropsies. The interstitial hemorrhage noted in the heart and bladder wall may be due to the intense congestion, or to a preceding violent heart action with vascular contraction and increased blood pressure. Direct action on the heart muscle is not unlikely, because in many of the rapidly fatal cases the drug undoubtedly obtained immediate access to the circulation either by application to raw surfaces or by urethral injection following attempts at catheterization when minute abrasions of the mucosa may have been produced, or by subcutaneous injection with the entry of the drug into a small vessel. The changes in the central nervous system may have been brought about by the preceding anesthesia.

The rapidity of action is noteworthy. Many of the accidental deaths encountered by physicians have followed intraurethral injections and usually there has been a history of slight bleeding. This would seem to indicate that the injured mucosa permitted the rapid absorption of comparatively large quantities of cocaine, with immediate action on the heart muscle and respiratory centre. When the drug is slowly absorbed, toxic symptoms may ensue but usually without fatal result. It has been noted by Sollmann that in the urethra of male dogs, larger quantities of local anesthetics are more rapidly absorbed and that the rapidity of absorption is most rapid during the first ten minutes. In a recent investigation on the comparative absorptive power for drugs of the urethra, Macht noted that urethra possesses greater absorptive power than the bladder, and that the posterior urethra absorbs more rapidly than the anterior urethra. He attributes this fact in part to the presence of glands, but in a previous paper,

Doctor Macht also shows that rapid absorption of cocaine may occur from such a surface as the vaginal mucosa where no glands are present.

The anesthetics often substituted for cocaine may also produce toxic symptoms. Thus Jacobs reports two cases of poisoning from the use of alypin in the urethra. In each instance 2 drams of a 2 per cent solution was used and slight bleeding was noted. In a few minutes after the injection there occurred violent convulsions, cyanosis, and weak pulse, but recovery followed. Jacobs concluded that more rapid absorption took place from a traumatized surface.

The variable quantity of cocaine stated as the cause of death would seem to indicate that some individuals are more susceptible than others. A method to detect this increased susceptibility would be highly valuable but does not appear possible at this time, since the true action of cocaine is not known (Kuroda) other than its paralyzing action on sensory end organs. Since characteristic symptoms are produced quite promptly, however, it might not be impractical to make a preliminary injection of a small dose and watch for signs of poisoning. This may be tried particularly in the urethral cases which in medical practice appear to have produced the greatest number of deaths.

In the fatal cases death occurs so promptly that little can be done to counteract the action of the drug. It has been suggested that alcohol or hyoscin hydrobromid be administered just prior to the injection of cocaine in order to prevent symptoms of poisoning. After symptoms have appeared, rapidly acting cardiac and respiratory stimulants are indicated.

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ACUTE ADRENAL INSUFFICIENCY*

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IT is now over a century since Addison first described the condition to which his name has been attached, a condition characterized by profound asthenia, low blood pressure, gastrointestinal disturbance, and a remarkable pigmentation of the skin and certain of the mucous membranes, associated generally with tuberculous destruction of both adrenal bodies. In the years which have elapsed a vast amount of work has been done upon the physiology of the adrenals, and one brilliant discovery has been made, but it can not truthfully be said that a single ray of light has been shed on the nature of the relationship which exists between disease of the adrenals and the symptom-complex of Addison's disease. It need cause no surprise, therefore, that the extraordinary condition to which the name acute adrenal insufficiency has been given should remain a complete mystery, for the function of the adrenals is still largely unknown.

Part of this ignorance is perhaps due to the fact that too much stress has been laid on the methods of the physiologic laboratory, with the result that the possibilities of morbid anatomy as an aid in elucidating these problems have been belittled or overlooked. As one of the leaders of physiologic thought has justly said: "The world of pathologic phenomena is nothing but an endless series of the most different and unusual combinations of physical occurrences which never make their appearances in the normal course of life. It is a series of physiologic experiments which nature and life institute, with such an interlinking of events as could never enter into the mind of the present-day physiologist, and which could scarcely be called into existence by means of the technical resources at our command. Clinical observation will consequently always remain a rich mine of physiologic facts."

The dual nature of the adrenals is well recognized. As in the case of the pituitary the gland consists of two parts which are perfectly distinct in development, in structure, and almost certainly in function. The cortex is developed from the mesoderm, the medulla, in conjunction with the sympathetic system, from the neural ectoderm. The cortex consists of columns of cells loaded with a doubly refracting lipoid material, an ester of cholesterin, which varies in amount in different physiologic and pathologic conditions. The medulla is part of the system of chromophil tissues, and contains the substance adrenalin.

The analogy to the pituitary is worth noting. In the pituitary there is a part—the pars posterior—which is composed of inert-looking, nonglandular material, and yet the extract prepared from it is one of the most powerful physiologic substances with which we are acquainted. The glandular anterior portion, the extract of which produces no remarkable effects, is, however, the part which is probably essential to life. In the adrenal the medulla produces an equally active substance, and the more glandular cortex appears to be correspondingly inert, but here again evidence is slowly accumulating which seems to indicate that the apparently inert part is the one vital to the individual.

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It is only in the mammal that these widely differing structures are found in the relation of cortex and medulla. In birds they occur as intermingling columns, and in elasmobranch fishes they are entirely distinct organs, the cortex being represented by an elongated interrenal body lying between the caudal ends of the kidneys, and the medulla by a succession of paired chromophil bodies. It may be, however, that the union of the two parts in the mammal may have for its object the functioning of the two parts as one organ. Of this we have no knowledge.

The discovery by Oliver and Schäfer that the medulla contains a substance of remarkable physiologic activity which acts upon the structures supplied by the sympathetic system, together with the therapeutic applications of this discovery, has served to focus attention, perhaps unduly, on this constituent of the gland, with the result that the cortex has been largely neglected.

At present we know nothing of the function of the cortex. It has been suggested that it exercises a control over sexual development, as the anterior lobe of the pituitary undoubtedly does. It is true that certain tumors of the cortex in children are associated with a remarkable precocity in the development of the sexual organs, and that similar tumors in elderly women may be accompanied by a development of male characteristics. It is possible also that the cortex may be intimately associated with the metabolism of lipoids, especially cholesterin. The fact remains, however, that we have no real knowledge on the subject.

Nor is there even agreement as to whether the cortex is essential to life. Some element of the gland certainly is necessary. Extirpation of one adrenal in the animal produces no effect, but removal of both adrenals is followed by death, generally in from two to four days. Attempts to remove the cortex alone or the medulla alone have failed to throw conclusive light on the subject, owing to the technical difficulties of the operation. The general view at present held is that it is to the loss of the adrenalin-producing substance that the fatal effect of complete adrenalectomy must be attributed. And yet removal by Biedl of the interrenal body, that is the cortex, in cartilaginous fishes, in which separation of the two systems is unusually well marked, was followed by asthenia and death.

This important question is therefore still undecided, and as the methods of experimental physiology have failed in this instance, it remains to be seen whether morbid anatomy can throw any light on the subject.

The relationship of the syndrome of Addison's disease to disease of the adrenals is well established, but of the nature of this relationship we have little real understanding, nor can it be said that recent physiologic research has furthered to any appreciable extent this understanding. It is impossible to reproduce the symptoms of Addison's disease in animals. The low blood pressure and lack of vasomotor tone are no doubt due to deficiency in adrenalin, but the cause of the muscular asthenia, the pigmentation, and the gastrointestinal disorder is still a matter for conjecture.

Further complicating the problem is the fact that cases of Addison's disease may occur with apparently healthy adrenals. In such cases there is often some degeneration of the chromophil tissue in relation to the abdominal sympathetic, and the great sympathetic ganglia may show pathologic changes of va-

rious kinds. Moreover there may be most extensive destruction of the adrenals without any symptoms of Addison's disease. An endeavor is usually made to explain away such anomalies by presupposing the presence of accessory adrenals, but if these bodies—which at best are minute in comparison with the adrenal itself—are as frequently present as has been claimed, it is remarkable that they do not come to the rescue in cases of typical Addison's disease.

The onset of the syndrome described by Addison is gradual. Adrenal insufficiency, however, may be acute instead of chronic in type, with a very different resulting clinical picture. The condition is named acute adrenal insufficiency, but that must not be taken to imply that it bears any definite relation to the symptoms of Addison's disease. It owes its name solely to the fact that the only constant lesion found is profound destruction of both adrenal glands. Of such a condition the following case is a striking example.

The patient, a soldier, thirty-eight years of age, was in Winnipeg on a few days' leave of absence. Up to the time of his leave he was performing the more or less arduous duties of a military training camp. It may therefore be assumed that he displayed no marked myasthenia nor other grave symptoms of organic disease. Early one morning he was found in a semiconscious condition in his room. A few hours later he was admitted to the Winnipeg General Hospital under the care of Doctor J. R. Davidson. By that time he was sinking into a state of coma. The picture was one suggestive of cerebral hemorrhage. The limbs were rigid, the reflexes gone, and the pupils distinctly dilated. The face and hands were cyanosed. The temperature was 99° F. Urine was drawn off and found to be normal. Lumbar puncture was done, but the cerebrospinal fluid showed no change and gave a negative Wassermann reaction. The patient died two and a half hours after admission. The clinical course was thus apoplectiform in type.

The autopsy was performed within two hours of death. Old adhesions were present over the liver, spleen, and mesocolon. Both pleural cavities were obliterated by old adhesions. There were fibrous nodules at the apices of both lungs, and a tuberculous cavity the size of a hazel nut in the apex of the right lung. The heart and kidneys were normal. The meningeal vessels were injected, and the cerebrospinal fluid somewhat increased in amount, but the brain showed absolutely no abnormality. The stomach contents when examined later showed no trace of poison.

The only organs exhibiting any marked pathologic change were the adrenals. These were almost entirely destroyed, and converted into structureless, amorphous, yellowish masses, firm in texture, and considerably larger than the original glands. On the right side no trace of adrenal tissue, either cortex or medulla, could be found. On the left a narrow strip of adrenal not more than 2 mm. in width was present at one point. This consisted entirely of cortex, the cells of which contained a lipoid substance which stained red with Scharlach R, but which was not anisotropic. The remainder of the gland consisted of areas of necrosis surrounded by the endothelial and giant cells characteristic of tuberculosis. No trace of medullary substance remained. Attached to the caseous mass was a small nodule which showed the microscopic structure of a sympa-

thetic ganglion. The nerve cells and fibres of this ganglion, stained by various methods, showed no abnormality, but there appeared to be some increase of fibrous tissue.

This case is worthy of study from various points of view. It appears effectually to dispose of the theory that the medulla of the adrenal is essential to life. The entire medulla must have been completely destroyed for a considerable length of time, and yet the patient was in sufficient physical vigor to engage in the full duties of a military camp. Hypertrophy of accessory chromophil substance may be invoked, but this does not invalidate the statement as it applies to the adrenal medulla.

The persistence of a small amount of cortical tissue on the left side certainly suggests that this is the part of the gland which is necessary for the maintenance of life, but that when it is reduced to a minimum the end may come with startling suddenness. It would appear that under some conditions extensive destruction of the cortex may occur without the production of manifest symptoms, owing to the compensatory action of that which remains. When the limit of that compensation is reached, however, the picture of acute adrenal insufficiency makes its appearance.

The case must certainly be classed as one of acute insufficiency of the adrenals. Of this condition four types have been described, chiefly by French authors.

1. The acute abdominal form characterized by severe epigastric pain, lumbar tenderness, vomiting, and profound shock. The clinical picture closely resembles that of acute hemorrhagic pancreatitis.

2. The cerebral form in which convulsions or the rapid onset of coma are the chief features.

3. The asthenic form marked by a rapid and profound asthenia terminating fatally in a few days.

4. A form in which sudden death occurs without premonitory symptoms, and in which the only lesion revealed by autopsy is complete destruction of the adrenals.

In the majority of the cases described in the literature the pathologic finding has been a sudden vascular lesion of the adrenals, either in the nature of a hemorrhage destroying the glands, or a thrombosis of the adrenal vessels. Thus Lavenson describes a case of the abdominal type in which there was thrombosis of both adrenal veins together with acute hemorrhagic necrosis of the glands. It seems probable that all of the abdominal type of cases are of this nature.

The cerebral cases may also be due to an acute hemorrhagic lesion, as in that of Laignel-Lavastine, where a man of thirty-six years, apparently in good health, fell unconscious and died in coma twelve hours later. Arnaud, however, describes a case with an almost identical clinical history, save that the patient lived for forty-eight hours, in which there was no recent lesion, but almost complete replacement of the adrenals by old hematomata and organizing hemorrhagic foci. Janowski and Stursberg also record cases of acute adrenal in-

sufficiency in which the lesion was of a chronic, probably a tuberculous, nature. In this class the present case must also be included.

To explain the relation between the pathologic changes in the adrenals and the extraordinary and dramatic clinical course of the case is beyond our powers. Such a failure, however, will at least serve the useful purpose of recalling to our minds the fact that there are still more things to be learned about the adrenals than are contained in our philosophy. The detailed study of adrenalin has led many to think that we understand the function of these bodies. In reality we are only just beginning to realize our ignorance.

Why such a case should display none of the usual symptoms of Addison's disease we do not know. To appeal to the comparatively unaltered abdominal sympathetic or to hypothetical accessory cortical adrenals is merely to hang a dark cloak over our ignorance. Nor do we yet know the function of the adrenal cortex. Theories unsupported by sufficient evidence mislead by creating a false impression of knowledge, and those which attribute to the adrenal cortex antitoxic and internal secretory functions certainly appear to fall into that category. We see that it is probably essential to life. Let us go no further until evidence has been accumulated which is worthy of the name. Only thus can sure progress be made, and in such progress physiology and morbid anatomy should walk hand in hand.

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LABORATORY METHODS

A CONVENIENT DILUTION CHART OF USE IN SEROLOGIC AND OTHER TESTS IN WHICH VARYING QUANTITIES OF REAGENTS ARE EMPLOYED*

By Loren B. Taber, Berkeley, Cal.

DURING the present international emergency, laboratories are finding themselves divested of technicians while the volume of work increases. The author has been under the necessity of training relatively unskilled helpers possessing only a high school education into making routine serologic tests, and has found that although in selected workers accuracy of technic has been acquired with relative ease, ability to figure dilution tables has been, as a rule, entirely lacking. The situation has been complicated by the fact that when standard serum controls are made, one is usually compelled to use the smallest possible quantities in order to conserve supplies.

In a laboratory in which large numbers of tests are made upon perhaps a dozen different sera requiring widely divergent dilutions, the figuring of each table by the one in general charge of the work is unnecessarily time-consuming. In such a contingency the accompanying chart has proved itself of decided value.

ROUTINE USE OF CHART

Certain values in routine tests are fixed and known to the assistant: total volume of serum-saline-antigen mixture per tube (D); fractional volume of serum mixture in one tube of serum-saline-antigen (E); volume of serum mixture in one tube of serum-saline-antigen (F). The one who lays out the work merely fills in the values for the final dilutions of serum in the finished test, and indicates the antigens to be used, together with the number of tubes of each antigen to be tested at each dilution. The assistant is then able to calculate independently the remainder of the values.

A SERUM DILUTION TABLE FOR A SIMPLE AGGLUTINATION TEST

As a practical example, let us consider an agglutination test (see Chart I) in which four dilutions of serum ,1/100, 1/200, 1/400, and 1/800, and twenty antigens are used. The customary total volume of serum-saline-antigen in one tube (D) mixture is 1 mil; the fractional volume of *serum mixture* in one tube of serum-saline-antigen (E) is 1/2; the volume of serum mixture in one tube of serum-saline-antigen (F) is therefore 0.5 mil. The values are now complete through F.

It is not necessary to calculate G as this value is not used in the final formulas.

*From the Serum Department, Cutter Laboratories, Berkeley, Cal.

The total volumes of the serum mixtures at the different dilutions (H) are found by multiplying the number of tubes at each dilution (C) by the volume for each tube (F). $C \times F = 20 \times 0.5$ mil $= 10$ mils.

For the last dilution, the total volume needed will be only that mixed with the antigens plus a minimum amount (1 mil) for the wetting of glassware. There $I^{IV} = 0$, and $J = H$ mils $+ 1$ mil $= 10$ mils $+ 1$ mil $= 11$ mils.

The volume of *serum* needed for each dilution (K) need be calculated only for column I, as in the final formulas for the following values it does not occur.

The calculation of the amounts of serum dilution and of saline to be mixed now proceeds as follows:

Serum dilution $H^{IV} \rightarrow J^{IV} \rightarrow L^{IV} \rightarrow I^{III} \rightarrow J^{III} \rightarrow L^{III} \rightarrow I^{II} \rightarrow J^{II} \rightarrow L^{II} \rightarrow I^{I} \rightarrow J^{I} \rightarrow K^{I}$.

Saline.—As the chart indicates, the amount of saline to be used in each flask (M) is found by simply subtracting the amount of the previous serum mixture to be used (L) from the total volume desired (J).

CHART I

A SERUM DILUTION TABLE FOR A SIMPLE AGGLUTINATION TEST

(A convenient table of use in making dilutions with minimum quantities of serum)

A	Number of serum dilution flask	I	II	III	IV
B	Final dilution of serum in serum-saline-antigen mixture	1/100	1/200	1/400	1/800
C	Number of test tubes at each dilution	20	20	20	20
D	Total volume in one tube of serum-saline-antigen mixture	1	1	1	1
E	Fractional volume of *serum mixture* in one tube of serum-saline-antigen	1/2	1/2	1/2	1/2
F	Volume of serum mixture in one tube of serum saline-antigen $= D \times E$	.5	.5	.5	.5
G	Mils of serum in one mil serum mixture $= \frac{B}{E}$	–	–	–	–
H	Mils of serum dilution needed for C tubes $= C \times F$	10	10	10	10
I	Mils of serum dilution needed for next dilution, plus a minimum amount for wetting of glassware = next whole number over L^{a+1} or more if the worker desires. In the last column $I = O$.	9.	.9	6.0	0
J	Mils of serum dilution needed, total $= H + I$. In the last column J = the next whole number over H, or more if the worker desires.	19	19	16	11
K	Mils of serum needed, total $= (G \times J) = \left\{ \frac{B}{E} \cdot J \right\}$	0.38	–	–	–
L	Mils of previous serum mixture needed $= \left\{ \frac{K}{G^{a-1}} \right\} = \left\{ \frac{B^a}{E^a} \cdot J^a \right\} \div \left\{ \frac{B^{a-1}}{E^{a-1}} \right\} = \left\{ \frac{B^a}{B^{a-1}} \right\} \times (J^a) \times \left\{ \frac{E^{a-1}}{E^a} \right\} = \left\{ \frac{B^a}{B^{a-1}} \times J^a \right\}$ *	See K	8.5	8.0	5.5
M	Mils saline $= J - L$. In the first column $M = J - K$	18.62	8.5	8.0	5.5

*When the values of E are a constant, as is customary in routine serum tests $\frac{E^{a-1}}{E^a}$ cancels out. If $\frac{B^a}{B^{a-1}}$ is made a constant such as 1/2, 1/3, 1/10, etc., a further simplification results. We must keep in mind that the ratio $\frac{B^a}{B^{a-1}}$ must be of such value that when multiplied by J^a the resulting quantity will be measurable in the available measuring devices.

MORE COMPLICATED DILUTIONS

The foregoing example is one of a very simple dilution in which it was desired to use an absolute minimum of serum while employing the standard volumes of antigen and serum-saline mixture. Concerning the more extended application of the chart, it is apparent that instead of *serum*, any liquid can be diluted; instead of *saline*, any diluent can be employed; and instead of *antigen*, an equal volume made up of any number of reagents can be substituted, one or all of which may have values which may vary within the limits of the experiment at the will of the operator.

A MODIFICATION OF THE WASSERMANN TEST*

By Clarence N. Callary, Philadelphia, Pa.

THE Wassermann test is now recognized as one of the most valuable laboratory aids that has yet been brought into routine use. The practitioners have long since come to recognize in this test a splendid method of syphilitic diagnosis and at the same time have come to regard its negative presence in many instances as a sore disappointment. It is not uniformly present in all cases of manifest syphilis from the clinical point of view. Is this a fault of the technic or is it due to a temporary or permanent disappearance in the reaction in certain persons and in certain phases of the infection, regardless of the application of specific medication? The answer as a result of experiences is that it is due partly to the first cause and partly to the second. I say this because I have been able to add to the column of positives by utilizing a modification of the classic Wassermann test which eliminates those errors inherent in the test itself. I maintain that Wassermann's original method is subject to an error arising from the presence in human serum of a varying amount of natural antisheep amboceptor capable of being reactivated by guinea pig complement. While the quantitative relations of the complement and antigen in the Wassermann reaction are important, they are vastly more so in the case of the hemolytic amboceptor. Noguchi[1] has pointed out very clearly the dangers of not delicately adjusting the quantity of amboceptor used in the reaction. Morgenroth and Sachs[2] have shown that the relationship between complement and amboceptor necessary for hemolytic reaction is one of inverse proportions. To state it more clearly, in their own words, "in the presence of larger quantities of amboceptor, smaller quantities of complement suffice" and vice versa. Noguchi, in his work, has found that, while, in the presence of one unit of amboceptor, 0.1 c.c. of guinea pig's complement is required to produce hemolysis, by using four, eight, and twenty units of amboceptor, complete hemolysis is obtainable with one-third, one-fifth, and one-tenth of the 0.1 c.c.

*From the Pathologic Laboratory, Garretson Hospital, Philadelphia, Pa.

[1]Proc. Soc. Exper. Biol. and Med., vi, 3, 1909.

[2]Morgenroth und Sachs in Ehrlich's Gesammelte, Arbeiten, etc., Berlin, 1904.

complement, respectively. For this reason an excess of amboceptor might result in complete hemolysis in a test, if a small fraction of the complement were left unfixed by the syphilitic antibody. Another result of an excess of amboceptor would consist in a partial dissociation of the complement from its combination with the antigen-antibody compound. As Noguchi puts it, "a quantity of syphilitic antibody just sufficient to fix 0.1 c.c. of the complement against two units of the amboceptor is no longer efficient in holding back the complement from partial liberation against the influence exerted by more than four units of the amboceptor." Human serum contains a certain quantity, and sometimes a large quantity, of amboceptor hemolytic for sheep red cells. From these considerations it follows that the serum from the patient must, in each case, be titrated in order to determine the hemolytic unit. For this purpose a number of mixtures are made in test tubes, containing each 0.1 c.c. of serum of patient (inactivated at 54 C. for 15 minutes), 0.2 c.c. of a 20 per cent complement (fresh guinea pig serum) and increasing quantities of a 5 per cent emulsion of sheep's red cells, thus:

TITRATION

TUBE	SERUM OF PATIENT	20% COMPLEMENT	0.85% NACL	5% S.R.C.	
1	0.1 c.c.	0.2 c.c.	0.5 c.c.	0.2 c.c.	Complete hemolysis
2	0.1 "	0.2 "	0.4 "	0.3 "	" "
3	0.1 "	0.2 "	0.3 "	0.4 "	" "
4	0.1 "	0.2 "	0.2 "	0.5 "	Partial "
5	0.1 "	0.2 "	0.1 "	0.6 "	No "

TEST

TUBE	SERUM OF PATIENT	ANTIGEN	20% COMPLEMENT	0.85% NACL	5% S.R.C.	
6	0.1 c.c.	0.1 c.c.	0.2 c.c.	0.5 c.c.	0.2 c.c.	?
7	0.1 "	——	——	0.5 "	0.2 "	Serum control
8	——	——	0.2 c.c.	0.5 "	0.2 "	Comp. "
9	——	——	——	0.5 "	0.2 "	Salt "

Controls show no hemolysis.

These tubes are placed in water-bath at 40° C. for one hour and following this, there are added to the test the required quantities of a 5 per cent emulsion of sheep's red cells (2 units) and again place test in water-bath at 40° C. for one hour, then make final reading. In the given case Titration tube No. 3 (0.4 c.c. of a 5 per cent S.R.C.) represents one unit, and one half or 0.2 c.c. of a 5 per cent emulsion of sheep's red cells, two units, are the quantities to be used for the test tubes 6 to 9.

In ten per cent of human serums in which no amboceptor is present to complete test add one unit of amboceptor (that has been titrated with 0.2 c.c. of a 20 per cent complement against 0.5 c.c. of a 5 per cent emulsion of sheep's red cells) and 0.25 c.c. of a 5 per cent sheep's red cells, thus:

TUBE	SERUM OF PATIENT	ANTIGEN	20% COMPLEMENT	0.85% NACL	5% S.R.C.	1 U. AMBO.
6	0.1 c.c.	0.1 c.c.	0.2 c.c.	0.5 c.c.	0.25 c.c.	"
7	0.1 "	——	——	0.5 "	0.25 "	"
8	——	——	0.2 c.c.	0.5 "	0.25 "	——
9	——	——	——	0.5 "	0.25 "	1 U. of Ambo.

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EDITORIALS

The Influenza in Germany

IT SEEMS from reports that have reached the office of the Surgeon General that epidemic influenza became sufficiently important in Germany last July to lead to special conferences of prominent medical men at Berlin and at Munich. We have no detailed information concerning the extent of the prevalence or the degree of virulence which the epidemic manifested in Germany. At the present time it seems that the virulent form of the disease first appeared in Germany. It is true that a mild epidemic of influenza passed through Spain in the early Spring of 1918, then visited France and probably extended into Germany; but in both Spain and France the Spring epidemic was mild resembling that form of the disease which we have had in this country more or less for some years, and which acquired a rather wide diffusion in the year 1916. The German pathologists who attended the conferences at Berlin and Munich evidently had had plenty of material under observation and upon which they reported and consulted. It was concluded at these conferences that the pathology of the epidemic then

prevalent in Germany was the same as that of the epidemic of 1889-90. This conclusion was reached after the comparison of preserved specimens from the epidemic of 1889-90 with tissues taken fresh from the body. Obendorfer stated that he had made a large number of autopsies at Munich and reported the lesions of the respiratory organs as uniform and typical to such an extent that he would undertake to dictate a protocol.

In the initial stage of the disease the most characteristic findings are bean-sized hemorrhages projecting into the lung tissue. This is followed by a firmer infiltration of the parenchyma, the nodules projecting against and raising the pleura. There are many intermediate formations between the small nodules and the large hemorrhagic infiltrations. There are all possible gradations from simple blood extravasations into the lung tissue, still containing air, to firm infarcts —the last mentioned consist of hemorrhages and have a bluish black tinge. The larger infiltrations are wedge-shaped with the base of the wedge projecting against the pleura, thus indicating their relationship to the vascular system. The extravasation of red blood cells seems to be due to abnormal permeability of the walls of the blood vessels.

The second stage is characterized by an exudative pneumonic process combined with hemorrhages. The picture varies considerably. There may be a true croupous hepatization of lobular, or even lobar, extent, both red and grey, though the tinge is usually brownish and not distinct. The surface is not dry, but is covered by a slimy, dirty coating, resembling a picture of Friedlander's pneumonia. The pneumonic foci are sometimes flattened out at the ends into yellowish white wedge-shaped structures corresponding to anemic infarcts both in form and in color. These often become the seat of gangrene or suppuration, the pleura being coinvolved in the process. In the majority of cases there is a catarrhal and desquamative infiltration rather than a fibrinous exudation. However, in the majority of instances, especially in the severe ones, there is marked suppuration.

The bronchi are filled with pus even in the first stage, the smaller branches contain thin fluid, though at times firm exudates plug the lumen of the smaller bronchi. The effect of this is distended bronchi. In some instances there are many minute abscesses surrounded by hemorrhages. These abscesses often become confluent, ending up in the formation of large pus cavities.

The first lesions in the pleura consist of pinhead hemorrhages, and empyema may result. As a rule only one side is affected. Pericarditis is a natural consequence of the inflammation of the pleura. There are no gross changes in the heart with the exception of some thickening of the arteries.

The larynx and the upper third of the trachea usually show no involvement, but the lower third of the trachea is the seat of an intense mucopurulent exudation, which in many cases assumes a fibrinous character, with the consequent formation of extensive pseudomembranes in the lower trachea and down into the bronchi. Sometimes edema of the epiglottis is observed.

A rather characteristic feature is presented by the hyperplastic condition of the lymphatic apparatus of the tongue and the tracheal ring. The thymus

is well preserved, the cervical and axillary, but not the inguinal glands, are enlarged. On the whole, the impression of the existence of a status thymo-lymphaticus is conveyed. As young individuals are mainly affected these facts may stand in the relation of cause and effect. The spleen is enlarged and sometimes a septic spleen tumor may be found.

The liver is but seldom involved, and the kidneys show a general hyperemic condition. In the brain and the meninges there is a marked vasodilatation, but no meningitis is found. Pinpoint hemorrhages are sometimes seen near the base of the brain.

The histologic examination reveals the following unusual findings: In the trachea there is an intense exudation of fibrin in the deep layers of the mucosa, and a progressive inflammation of the deeper portions of the tracheal walls. In the lymphatic glands there is an enormous vasodilatation with hemorrhages, as well as proliferation of the endothelium, especially in the axillary glands.

The foci of inflammation in the lungs show a leucocytic infiltration round the alveoli, bronchi, and the walls of the small arteries. It does not involve the whole vessels, which are dotted with isolated spots of infiltration. There are also hemorrhages into the heart valves, with a consequent displacement of the fibers and damage to the endothelium with no definite endocarditis, but with lesions which facilitate the development of a secondary mycotic endocarditis. There are, therefore, signs of lesions of the walls of the vessels, which are found to be particularly marked in some cases in the pulmonary artery. An advanced mycotic arteritis was detected in these cases. Masses of streptococci were found.

Obendorfer concludes his report with the following statement:

"The essence of the whole pathologic picture consists, therefore, in the abundance of hemorrhages seen in the mucous and serous membranes, in the respiratory tract, and in the lungs, which indicate a damaged condition of the capillary vascular system. The abscesses, save for those originating in the bronchi, are also of a hematogenic nature. The whole process seems to be primarily a bacteriemia localized in particular in the pulmonary blood-vessels. Hemorrhages in the lungs pave the way for a secondary infection, the results of which dominate the whole field in the later stages. In any case the wedge-like shape of the pulmonary foci indicate a vascular origin of the lesions. From a purely anatomical point of view the condition bears many points of resemblance with pneumonic plague, though there is no indication as to an entry of the virus through definite lymphatic channels. The primary bacteriemic condition was not found to be due to B. influenza (Pfeiffer), and thus the invading virus remains undiscovered."

It is worthy of note that in Germany and in this country most of the deaths due to pneumonia following influenza have been among the most robust and most vigorous men. This is quite characteristic of all pestilences. The severe, rapid infectious diseases kill most quickly and most surely the strongest and most robust. This is the case not only in pandemic influenza, but in the

plague, typhoid fever, typhus fever, smallpox, and in short, all the acute, highly infectious diseases. This is explained by the resistance put up by the body cells against the invading microorganisms. A strong and vigorous man attacked by one of these diseases either makes a speedy and rather abrupt recovery, or is likely to die. Nature overdoes the resistance, kills the invading organisms too rapidly and sets free such an amount of poison that death results.

In many of the reports coming into the Surgeon General's Office it is noted that the mortality is high among the most vigorous men. Moreover, this epidemic differs materially from the ordinary influenza in the age incidences of those who die. In the ordinary influenza, children and the aged furnish the greatest number of deaths; while in the pestilential form of the disease most of the deaths are among those from twenty to forty years of age. It has been assumed by some that the infectious diseases, in the long run, benefit the race by killing off the weaklings. Even Herbert Spencer, the great philosopher of modern science, taught this doctrine; but the epidemiologist knows better. Infection, like war, kills the young, vigorous, robust adults.

—*V. C. V.*

Notes on Influenza

1. Pandemic influenza is an acute infectious disease, of unknown causation, characterized by a marked leucopenia which removes the normal barriers against infection and exposes the body to invasion by whatever pathogenic organisms may gain access to it.

2. It may cause death without the aid of other viruses, but in the majority of instances its deleterious effects are intensified by the presence and activity of other pathogenic organisms.

3. In its spread it is not dependent upon the presence or aid of other viruses. It attacks the strong and vigorous as readily as it does the infirm. The mortality caused by it is higher among the strong and vigorous than among the weak and sickly.

4. The mortality accompanying or following it is largely determined by the presence and virulence of other infectious organisms.

5. The period of incubation, so far as it can be determined, is two days or less depending, doubtlessly upon the virulence and the amount of the virus introduced into the body and the readiness with which the natural resistance of the body is broken down and the degree of defenselessness, indicated by the leucopenia, established.

6. The pathogenic organisms which most frequently take advantage of the defenseless state of the body induced by the influenza virus are those which are capable of growth and multiplication in the pulmonary tissue, such as the different types of pneumococcus, streptococcus, Friedlander's organisms, and possibly some varieties of staphylococcus and the Pfeiffer bacillus.

7. Punctures made from the lungs during life and during the active stage of the pneumonia may show any of the above-mentioned organisms, either in

pure culture or in mixed form. The question arises as to how far these organisms may be due to terminal infection.

8. The pathologic condition found in the lungs after death from pneumonia following influenza, is determined by the invading organisms.

9. Influenza is not transmitted through the air for long distances, nor is it due to weather, nor to meteorological conditions. It is transferred from man to man either directly or indirectly; either by direct contact or indirect contact.

10. In the epidemic of 1889-90, fifteen hundred deaths in New York City were attributed to influenza. This does not mean that the influenza virus alone and unaided caused this number of deaths, but is does mean that during the period of the epidemic the normal deaths were increased by this number. In Massachusetts, Abbott says in speaking of that epidemic, that 39 per cent of the population were affected. It was less prevalent in Southern than in Northern cities. It was not only less prevalent in the South, but less fatal. In Massachusetts the disease appeared earlier and was more fatal in the more intensely populated areas of that state. The ratio of deaths to the population of the state at large was about 12 per ten thousand; to those attacked it was 31 per ten thousand. The epidemic of 1889-90 was the most fatal scourge that had visited Massachusetts up to that time. It lasted about fifty days and increased the mortality in that state by about twenty-five hundred.

11. Speaking of the epidemic of 1889-90, Abbott, Secretary of the Massachusetts State Board of Health, (See Twenty-first Annual Report of the State Board of Health of Massachusetts) formulated the following conclusions:

"1. The first appearance of the influenza in Massachusetts as an epidemic, in the past season, may be stated to have been on the 19th or 20th of December, 1889, and the place of its first appearance was Boston and its immediate neighborhood.

"2. It increased rapidly in the number of persons attacked, and reached its crisis generally throughout the state in the week ending January 11, 1890, after which date it gradually declined in severity, and had nearly ceased as an epidemic by the 10th of February; so that the duration of the epidemic was about seven weeks. It reached its crisis earlier by several days in Boston than in the smaller cities and the remoter parts of the state. Its course was still later in Nantucket, Dukes and Barnstable counties.

"3. The ratio of the population attacked was about 40 per cent,—or more exactly, as indicated by the returns, 39 per cent,—or about 850,000 persons of all ages.

"4. People of all ages were attacked, but the ratio of adults was greatest; of old people next, and of children and infants least.

"5. The weight of testimony appears to favor the statement that persons of the male sex were attacked in greater number and with greater severity than females.

"6. The average duration of the attack (acute stage) was from three to five days.

"7. The predominant symptoms were mainly of three general groups,—

nervous, catarrhal and enteric, the last being much less common than the others; the special symptoms most observed in the nervous group being extreme depression, pain and weakness; in the catarrhal group, cough, dyspnea and coryza; and in the enteric group, nausea, vomiting and diarrhea.

"8. The chief diseases which followed in the train of influenza, and were intimately associated with it, were bronchitis and pneumonia. Phthisis, when already existing in the victim of the attack, was undoubtedly aggravated; and, in many cases, a fatal termination was hastened.

"9. The ratio of persons attacked in industrial and other establishments employing large numbers was about 35.5 per cent, or less than that of the population at large. That of the inmates of public institutions was still less, —29 per cent.

"10. The ratio of persons who were obliged to leave their work on account of illness from influenza was about 27 per cent of the whole number employed.

"11. The average length of their absence from work was five days.

"12. Special occupations do not appear to have had a marked effect in modifying the severity of the epidemic upon operatives in such occupations.

"13. Various theories have been advanced relative to the method of propagation or spread of influenza."

Dr. Abbott concluded, after considering the various theories concerning the spread of the disease, that it does not travel faster than the modern modes of locomotion can explain. The conclusion, therefore, is that human intercourse is the all important factor in the transmission of this disease.

12. Lord (*Journal Medical Research*, 14, 295) found Pfeiffer's bacillus in pure culture in 25 per cent, and mixed with other organisms in 59 per cent of 186 cases in an interepidemic period; while he found it in pure culture in 15 per cent and with other organisms in 35 per cent of 20 cases during an epidemic. This epidemic prevailed in Boston from the last week in November, 1907, to the middle of January, 1908. "It appears to be certain for New England at least, that a larger proportion of the population was attacked than in any previous outbreak of acute respiratory infection since 1889-92."

13. In 1916, influenza seems to have increased. In the vital statistics report for that year this disease is accredited with 18,886 deaths. However, it is uncertain how many of these deaths were due to some form of pneumonia. In the annual report of the Department of Health of the State of New York for 1916, there appears the following statement:

"Notwithstanding the epidemic of influenza and infectious colds that visited the city the early part of the year, and the epidemic of anterior poliomyelitis that visited the city during the summer, the death rate was the lowest on record."

14. Park (*New York Medical Journal*, October 12, 1918) has found the influenza bacillus in "almost every case of clear-cut infectious influenza. In the complicating pneumonia we have found them associated with either strepto-

coccus or pneumococcus. In one case bronchopneumonia was due entirely to the influenza bacillus."

15. Symmers (Ibid) calls attention to the fact that the disease kills the robust as well as the weak. He states that the disease begins in the lower lobes. "The sequence of events is that the infective organisms, acting first and particularly simultaneously upon the lower lobes of both lungs, cause a rapidly confluent variety of lobular exudative pneumonia attended by changes in the vascular structures marked by the escape into the alveoli of variable numbers of red cells and quantities of blood serum, either independently of one another or in combination." He states that no fibrin is found in the alveoli, that the lower lobes have a slate-blue color, that they are almost completely consolidated, the edges escaping consolidation, but undergoing corresponding emphysematous changes.

16. Berg and Bullowa (Ibid.) give the symptomatology, but do not mention cyanosis or epistaxis, which have been so frequently observed by others.

—*V. C. V.*

Ravages of the Influenza Epidemic

THE Bureau of the Census, Department of Commerce at Washington reports that influenza deaths in America greatly outnumbered the war's casualties among American troops.

"The influenza epidemic has thus far taken a much heavier toll of American life than has the Great War. The total loss of life throughout the country is not known, but the Bureau of the Census has been publishing, for 46 large cities having a combined population estimated at 23,000,000, weekly reports showing the mortality from influenza and pneumonia. These reports, which cover the period from September 8 to November 9, inclusive, show a total of 82,306 deaths from these causes. It is estimated that during a similar period of time the normal number of deaths due to influenza and pneumonia in the same cities would be about 4,000, leaving approximately 78,000 as the number properly chargeable to the epidemic.

"The total casualties in the American Expeditionary Forces have recently been unofficially estimated at 100,000. On the basis of the number thus far reported, it may be assumed that the deaths from all causes, including disease and accidents, are probably less than 45 per cent and may not be more than 40 per cent of the total casualties. On this assumption, the loss of life in the American Expeditionary Forces to date is about 40,000 or 45,000.

"Thus, in 46 American cities having a combined population of only a little more than one-fifth the total for the country, the mortality resulting from the influenza epidemic during the nine-weeks' period ended November 9 was nearly double that in the American Expeditionary Forces from the time the first contingent landed in France until the cessation of hostilities.

"For the 46 cities taken as a group, the epidemic reached its height during

the two weeks ended October 26, for which period 40,782 deaths were reported —19,938 for the week ended October 19 and 20,844 for the following week. Since October 26, however, the decline has been pronounced. During the week ended November 2, 14,857 deaths occurred, and during the following week only 7,798. The only city in which the number of deaths reported for the week ended November 9 exceeded the number occurring during the previous week was Spokane, Washington.

"In general, the epidemic traversed the country from east to west. In a number of eastern cities—notably Boston, where the greatest mortality occurred during the week ended October 5—the largest numbers of deaths were reported for earlier periods than that which covered the height of the epidemic for the 46 cities taken as a group. On the other hand, in New Haven, New York, Pittsburgh, and Rochester the maximum mortality occurred somewhat later than in eastern cities generally. In Baltimore, Buffalo, and Philadelphia the two-weeks' period ended October 26 showed the greatest number of deaths. For the entire nine-weeks' period, the greatest mortality due to the epidemic, in proportion to population—7.4 per one thousand—occurred in Philadelphia; and the next greatest—6.7 per one thousand—was reported for Baltimore."

The Pneumonias

WHILE our knowledge of acute inflammation of the lungs, known as pneumonia, is still meager and wholly lacking in many particulars, we are justified in at least tentatively and timidly making some suggestions. During the Spanish-American war we recognized typhoid fever and included all of a certain group of diseases under this designation. We now distinguish between typhoid and the paratyphoids, and of the latter we know that there are at least two. We distinguish between the bacilli causing the typhoidal diseases and we know that a vaccine which protects against typhoid does not protect against paratyphoid, and vice versa. The facts seem to justify us now in using the word pneumonia in the plural, and in speaking of the pneumonias. Of the pneumococcus there are at least four types, and possibly many more. Then there seems no doubt that the streptococcus does cause both lobar and bronchopneumonia. How many types of this organism are capable of causing pneumonia we do not know. There are cases of pneumonia in which Friedlander's bacillus is found in pure culture, and some pathologists are quite sure that this organism induces characteristic lesions which distinguish pneumonia due to this bacillus from the pneumonias due to other bacteria. During the prevailing influenza pneumonia skilled observers have obtained pure cultures of Pfeiffer's bacillus from the lungs by puncture during life. In the present state of our knowledge we may say that pneumonia may result from the growth in the lungs of the following bacteria:

(1) The pneumococcus of which there are at least four known types,

(2) The streptococcus of which there are many types, the hemolyticus apparently being the most virulent,

(3) The Friedlander organism.

(4) The Pfeiffer bacillus.

There is some evidence that a staphylococcus may cause pneumonia. Then, we must add the more specific pneumonia caused by the plague bacillus and which is believed to cause 100 per cent mortality.

We are beginning to realize that any bacterium which is capable of growth and multiplication in living lung tissue may be the cause of pneumonia. When such an organism multiplies in pulmonary tissue and sensitizes the body cells, the body cells begin to destroy the involving bacterial cells and the result of this change is the liberation of the protein poison with local inflammation and systemic poisoning. The poison set free is the same whatever the name or character of the invading bacterium may be.

If this conclusion be true, to what extent and from what cause may we reasonably expect the lesions to vary with variations in the kind of bacterial growth in the lung? This is an important question, and the following tentative explanation is offered. Each bacterium has its predilective tissue upon which it feeds. No living thing can grow and multiply without access to food, and nothing is food to a given organism unless it furnishes elements which can be prepared, absorbed and assimilated by the cells of that organism. As a result of this fundamental and basic biological fact we may expect that the widely different complex tissues of the lung will vary in their suitability as food supply to the widely different invading cells. When we recall that Pasteur showed that certain bacteria act upon one form of tartaric acid and are wholly without action upon another, the two differing only in the relative arrangement of their atoms, we gain some adequate comprehension of the essential relationship between food and consumer, between nutritive medium (whether it be natural and a constituent of the living body or artificial and in the test tube)—and the organism which it supports. Whether the pneumococcus, the streptococcus, the Pfeiffer bacillus and other organisms, each selects some histologic element in the lung tissue upon which it feeds, in which it multiplies and in which it is broken up by the sensitized body cells, we do not know. The solution of this question should be one of the problems constantly held in mind by those who are now studying the pathology of pneumonia. Since in most cases the infection is a mixed one, this problem will not be easy of solution. At present it is certainly difficult to name the infecting agent from a study of the lung tissue after death. Still there are some suggestive findings. It is well known that the Pfeiffer bacillus will not grow on artificial culture media unless hemoglobin be present and the fact that hemorrhages into the lung tissue and in other parts of the body are more common in influenza pneumonia than in other pneumonias may have some meaning. The fact that typical lobar pneumonia is most commonly associated with some type of the pneumococcus and

that the streptococcus is often present in bronchopneumonia may have a significance not hitherto attached to them.

The purpose of this writing is to make the claim that so far as the bacteriologic factor is concerned there are many species of bacteria which may cause pneumonia, and in this sense there are many pneumonias.

—*V. C. V.*

Why We Should Join the Red Cross

HOW American Red Cross physicians engaged in relief work in Jerusalem are accomplishing worth-while results in the face of great difficulties—and what they are up against, is shown in a report just received here from W. S. Dodd, A.R.C., physician working at Mejdel.

With two capable English trained nurses, and three native helpers, more or less useful, Dr. Dodd, his "hospital" housed under tents, performed 252 operations in seven weeks, besides giving medical examinations, treatment and counsel to hundreds of the destitute inhabitants and refugees.

His report says in part: "The work of the hospital was of the plainest sort, it might be called primitive. About twenty-five tents comprised the hospital proper, with a dispensary tent, and tents for the living quarters of the staff.

"The soil was all the purest sea-sand with thistles and scant grass; going barefoot was the universal custom, and in our own quarters we of the staff used to follow that custom with great pleasure. * * * *

"The professional side of the work was of the greatest interest to me and every day was a pleasure. The clinics numbered sixty to a hundred a day. Of course, we had all classes of cases in medicine and general surgery, but by far the larger proportion of our patients were eye-cases.

"Of the 252 operations that I did in less than seven weeks, 222 were for the eyes. This is the number of persons operated on, most of them having more than one operation, perhaps on all four lids, so that I really operated on 408 eyes.

"There were some cataracts, not more than would be seen in the same number of cases elsewhere, but trachoma and its consequences accounts for almost all of the eye troubles in this land. I set out to treat these cases radically and secured fine results when I could keep the patients long enough for a reasonable after-treatment. But even so, the number of eyes that can be saved from partial and total blindness is large and the economic value of each eye thus saved is enough to make the prosecution of this line of work of the greatest importance for the redemption of the land.

"The accident cases are always interesting. I had the last end of treatment of some cases of bombed hands, of which there had been quite a number in the earlier days. These were largely in children, and were due to their picking up unexploded Turkish bombs that were lying in the fields from the time of the British advance in the Gaza region. Many fingers and even hands were lost from this cause.

"Vermin was the great enemy we had to fight. Fleas were hardly counted as a problem because we could do nothing against them, they were everywhere and inevitable, and so far as we know at present not being the carriers of any special disease, did not come within the hostility of a medical conscience.

"Lice and maggots were a daily terror. How many wounds and injuries came to us filled with maggots I can not tell. A favorite dressing for a wound is a piece of raw meat, a breeding place for maggots, and they can hardly be blamed for invading the adjoining premises.

"Many a child had to be put under chloroform in order to search out and pull from their hiding places deep in the middle ear a half dozen wriggling maggots whose every motion was causing torture to the innocent victim.

"A woman came to the clinic complaining of headache. A single sore on her face led to questioning, and when she rather unwillingly undid her turban we found an exaggerated case of impetigo, and every separate sore was as if the whole thickness of the scalp down to the bone had been punched out, and every sore was a nest of maggots. I removed 60 at the first seance, and at the first dressing next day the nurse had more to do. The headache was cured without further treatment. And these are not the most loathsome cases that we saw.

"Another great difficulty with which we had to contend was the filthy habits of the people. In spite of providing proper sanitary facilities, we were compelled to have a scavenger go around every morning and clean up the filth from around the tents of the patients. The women were as bad offenders as the men. We made it a rule that anyone known to have violated these simple sanitary regulations must go without their dinner next day, and this was quite an effective punishment."